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Closing the Regulatory Gap for Synthetic Nicotine Products

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CLOSING THE REGULATORY GAP FOR SYNTHETIC NICOTINE PRODUCTS

PATRICIA J. ZETTLER, NATALIE HEMMERICH & MICAH L. BERMAN

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Abstract: In July 2017 the U.S. Food and Drug Administration announced a new “comprehensive plan for tobacco and nicotine regulation.” This plan focuses on making cigarettes less addictive while facilitating the development of alternative, and less-harmful, nicotine-containing products. This approach holds promise, and the public health stakes could not be higher—smoking is the leading cause of preventable death in the United States, resulting in roughly 480,000 deaths per year. But a new consumer product is emerging that could upset the FDA’s plans for a well-balanced regulatory scheme: synthetic nicotine. Synthetic nicotine products currently fall into a regulatory gap because they do not appear to meet the Federal Food, Drug, and Cosmetic Act’s definition of a tobacco product. If this gap remains in place, it is likely that more companies will choose to market synthetic nicotine products in order to evade regulation, undoing the potential benefits of the FDA’s plan for tobacco and nicotine regulation. This Article argues that the FDA can, and should, address this problem by regulating synthetic nicotine products as drugs. After reviewing the science of nicotine addiction and the FDA’s past and present regulatory schemes for nicotine, this Article explains how the FDA could establish that synthetic nicotine products are drugs under the FDCA’s definition. This Article then concludes with a discussion of the policy benefits of categorizing synthetic nicotine products as drugs.

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INTRODUCTION

In July 2017, the U.S. Food and Drug Administration (“FDA”) Commissioner, Scott Gottlieb, announced a new “comprehensive plan for tobacco and nicotine regulation,” intended to “place[] nicotine, and the issue of addiction, at the center of the agency’s tobacco regulation efforts.”¹ The FDA’s plan recognizes that although nicotine use carries some risks, it is “not *directly* responsible for the cancer, lung disease, and heart disease that kill hundreds of thousands of Americans each year.”² Nicotine makes tobacco products addictive, but it is these products’ other toxic and carcinogenic components, combined with their addictive properties, that make them deadly.³ Cigarettes are particularly lethal: they kill more than half of their long-term users.⁴ But because cigarettes are extremely effective at delivering nicotine quickly to the brain, they are also by far the most popular tobacco product.⁵

Based on these insights, the FDA is proposing a “Nicotine-Focused Framework for Public Health” that seeks to make the most deadly forms of tobacco use (i.e., cigarettes and other combustible products) less addictive while simultaneously encouraging the development of less harmful ways to deliver nicotine to those already addicted.⁶ These are laudable aims, and the public health stakes could not be higher. Smoking is currently the leading cause of preventable death in the United States, resulting in roughly 480,000 deaths per year—appreciably more deaths than other high-profile, significant public health problems, such as drug misuse and overdose.⁷ If cigarettes were gradually phased out and replaced by less harmful forms of nicotine use, it is

¹ *News Release, FDA Announces Comprehensive Regulatory Plan to Shift Trajectory of Tobacco-Related Disease, Death*, FOOD & DRUG ADMIN. (July 28, 2017) [hereinafter *FDA Comprehensive Plan*], <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm568923.htm> [<https://perma.cc/V9XW-AJB7>].

² Scott Gottlieb, Comm’r, U.S. Food & Drug Admin., *Protecting American Families: Comprehensive Approach to Nicotine and Tobacco* (July 28, 2017) (emphasis added), <https://www.fda.gov/NewsEvents/Speeches/ucm569024.htm> [<https://perma.cc/H6DM-YVC8>].

³ *Id.*

⁴ Scott Gottlieb & Mitchell Zeller, *A Nicotine-Focused Framework for Public Health*, 377 NEW ENG. J. MED. 1111, 1111 (2017).

⁵ *See id.*

⁶ *Id.* at 1111–12.

⁷ *See Smoking & Tobacco Use: Fast Facts*, CTRS. FOR DISEASE CONTROL & PREVENTION (updated Feb. 20, 2018), https://www.cdc.gov/tobacco/data_statistics/fact_sheets/fast_facts/index.htm [<https://perma.cc/6JAL-E33L>] (documenting number of tobacco related deaths); *Overdose Death Rates*, NAT’L INST. ON DRUG ABUSE (updated Sept. 2017), <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates> [<https://perma.cc/2E2T-4PB2>] (logging the total number of drug related deaths in the United States in 2017 at around 64,000).

quite possible that “the great majority of tobacco-caused diseases and deaths will disappear”⁸

The 2009 Family Smoking Prevention and Tobacco Control Act (“TCA”), which granted the FDA powerful regulatory tools for tobacco products, represented an important step toward addressing this public health problem.⁹ Although the health harms of tobacco use have been well established for decades, it was not until passing the TCA that Congress gave the FDA broad authority to regulate the manufacture, sale, and marketing of tobacco products. In 2016, the FDA finalized a rule (referred to as the “Deeming Rule”) that extended its regulatory authority to all products meeting the TCA’s statutory definition of a tobacco product, notably including electronic cigarettes (“e-cigarettes”).¹⁰ Between the TCA and the later Deeming Rule, the FDA now has the authority to regulate all products “made or derived from tobacco that [are] intended for human consumption”¹¹

If the FDA is seeking to “comprehensively” regulate nicotine, however, there is still a notable regulatory gap: synthetic nicotine.¹² In just the past

⁸ Richard A. Daynard, *Doing the Unthinkable (and Saving Millions of Lives)*, 18 TOBACCO CONTROL 2, 2 (2009).

⁹ See Family Smoking Prevention and Tobacco Control Act, Pub. L. No. 111-31, 123 Stat. 1776 (2009).

¹⁰ See Deeming Tobacco Products to Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products, 81 Fed. Reg. 28,974, 28,974 (May 10, 2016) (to be codified at 21 C.F.R. pts. 1100, 1140, 1143) [hereinafter Deeming Rule]. As might be expected, the FDA’s decision to deem all products meeting the TCA’s definition of a tobacco product to be subject to its scheme for tobacco regulation is not without its critics—both from those who think it oversteps the government’s proper role and from those who think it does not go far enough to protect public health. See Micah L. Berman & Y. Tony Yang, *E-cigarettes, Youth, and the US Food and Drug Administration’s “Deeming” Regulation*, 170 JAMA PEDIATRICS 1039, 1039 (2016) (taking the latter approach); Jonathan H. Adler, *Why FDA Regulations Limiting E-cigarette Marketing May Cost Lives and Violate the Constitution*, WASH. POST (Dec. 12, 2017), https://www.washingtonpost.com/news/voikh-conspiracy/wp/2017/12/12/why-fda-regulations-limiting-e-cigarette-marketing-may-cost-lives-and-violate-the-constitution/?utm_term=.819c00cea3ee [<https://perma.cc/QPA6-PVPZ>] (taking the former approach). The merits of the Deeming Rule, however, are outside the scope of this Article.

¹¹ Deeming Rule, 81 Fed. Reg. at 28,976. The definition also includes components, parts, and accessories of tobacco products and excludes products that are classified as drugs or devices under the Food, Drug, and Cosmetic Act, even if those products are made or derived from tobacco. *Id.*

¹² Currently, the only nicotine not made or derived from tobacco that appears to be sold for human consumption is synthetic nicotine. There are, however, other potential non-tobacco nicotine sources. For example, tomatoes, eggplants, and other vegetables contain nicotine in small quantities. See, e.g., Michelle Castillo, *Eating Nicotine-Containing Produce Like Peppers, Tomatoes May Lower Parkinson’s Risk*, CBS NEWS (May 9, 2013), <https://www.cbsnews.com/news/eating-nicotine-containing-produce-like-peppers-tomatoes-may-lower-parkinsons-risk/> [<https://perma.cc/Z3ZA-CG84>]. Although it may not be economically feasible to derive nicotine from these sources at this time, if the FDA decides to regulate synthetic nicotine as a drug, it can—and should—make clear that its authority covers all non-tobacco sources of nicotine intend-

few years, synthetic nicotine—which is synthesized through chemical reactions in a lab—has entered the consumer marketplace, primarily as an ingredient for use in e-cigarette liquids.¹³ The sellers of such synthetic nicotine products celebrated the FDA’s acknowledgement that it may not be able to regulate such products under the TCA, because they are not “made or derived from tobacco”¹⁴ This leaves a regulatory gap that may become much more significant as the FDA begins to regulate e-cigarettes and as the price of synthetic nicotine continues to fall.

Sellers of synthetic nicotine products, though, are perhaps celebrating their escape from regulatory oversight prematurely. Although the FDA is

ed for drug uses, to deter future attempts to evade regulation. Likewise, the tobacco industry has long conducted research regarding the possibility of developing nicotine analogues “to circumvent . . . nicotine regulation.” Rosemary Vagg & Simon Chapman, *Nicotine Analogues: A Review of Tobacco Industry Research Interests*, 100 ADDICTION 701, 701 (2005); see also STANTON A. GLANTZ ET AL., *THE CIGARETTE PAPERS* 97–100 (1996) (describing the tobacco industry’s interest in nicotine analogues). The FDA, therefore, might also make clear that products containing nicotine analogues may be subject to regulation as drugs. For the purposes of this Article, synthetic nicotine is specifically addressed, but all arguments and policy implications apply with equal force to any other non-tobacco sources of nicotine and nicotine analogues that are intended for drug uses.

¹³ Although synthetic nicotine has long been sold in products not intended for human consumption, such as insecticides, it is only recently that the substance has been marketed for human consumption in e-liquids and other products. See, e.g., Florence F. Wagner & Daniel L. Comins, *Recent Advances in the Synthesis of Nicotine and Its Derivatives*, 63 TETRAHEDRON 8065, 8065, 8080 (2007). When this Article refers to “synthetic nicotine” or “synthetic nicotine products,” it is generally referring only to products intended for human consumption.

¹⁴ 21 U.S.C. § 321(rr)(1) (2012); see also Matt Rowland, *Will Synthetic Nicotine Save Vaping Industry from FDA E-Cig Regulations?*, VAPES (June 28, 2016), <https://www.vapes.com/blogs/news/will-synthetic-nicotine-save-vaping-industry-from-fda-e-cig-regulations#> [<https://perma.cc/BMQ9-4KFW>] (asserting that the FDA does not regulate synthetic nicotine products as tobacco products). There might be a colorable argument that, by giving the FDA jurisdiction over products “made or derived from tobacco,” Congress intended the FDA to regulate as tobacco products all tobacco-like products, including synthetic nicotine products. Indeed, synthetic nicotine is chemically identical to tobacco-derived nicotine, there do not appear to be scientific or public health reasons for regulating it differently than tobacco-derived nicotine, and in many instances courts have been willing to construe the FDA’s statute broadly in light of the agency’s public health mission. See *infra* notes 103–114, 211–230 and accompanying text. There are obvious legal vulnerabilities to the agency interpreting “tobacco product” to include synthetic nicotine products, however, because the plain language of the statute defines tobacco products as those “made or derived from tobacco” 21 U.S.C. § 321(rr)(1). This Article does not analyze whether the FDA could advance such an interpretation. Rather, this Article demonstrates that the FDA need not adopt such a vulnerable interpretation to properly regulate synthetic nicotine products because there is a strong argument that synthetic nicotine products are drugs. Moreover, as a practical matter, the FDA appears to have declined to interpret “tobacco products” so broadly as to include nicotine products not derived from tobacco. See *Commonly Asked Questions: About the Center for Tobacco Products*, FOOD & DRUG ADMIN. (Mar. 30, 2018), <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/AbouttheCenterforTobaccoProducts/ucm378205.htm#14> [<https://perma.cc/CUC5-3V37>].

likely unable to regulate synthetic nicotine products as tobacco products under the TCA, the agency could potentially regulate them as *drugs* under the Federal Food, Drug, and Cosmetic Act ("FDCA").¹⁵ To establish that a synthetic nicotine product is a drug, the FDA would have to show that the product is "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" or "intended to affect the structure or any function of the body"¹⁶ The FDA's authority to regulate synthetic nicotine products as a drug thus hinges on the meaning of "intended use" and the kinds of evidence that the FDA may use to demonstrate a product's intended use—issues that have long been controversial.

This Article argues that the FDA can and should regulate synthetic nicotine products as drugs under the FDCA. Diving into the legal history on "intended use," we demonstrate that although the case law on some key points remains unsettled, the FDA can make a convincing legal case that synthetic nicotine is best characterized as a drug under the FDCA. That is, there appears to be good evidence that the sellers of synthetic nicotine products generally intend those products to address disease or affect the structure or function of the body.¹⁷ Then, as a policy matter, we explore why the FDA *should* regulate synthetic nicotine products as drugs—arguing that such regulation would enable the agency to treat like products similarly, protect consumers, and encourage research innovation.

This Article proceeds in three parts. Part I provides background on the biological effects of nicotine, the FDA's history of tobacco and nicotine regulation, and the emergence of synthetic nicotine as an ingredient in products for consumer nicotine consumption.¹⁸ Part II discusses the FDA's legal authority to regulate synthetic nicotine products as drugs.¹⁹ Part III lays out the public policy and public health reasons for the FDA to do so.²⁰

I. HOW WE GOT HERE: UNDERSTANDING NICOTINE AND THE FDA'S NICOTINE-RELATED JURISDICTION

In 1994, the seven major tobacco company CEOs all testified before a congressional hearing that they believed nicotine was not addictive.²¹ This

¹⁵ See 21 U.S.C. § 321(g)(1).

¹⁶ *Id.* § 321(g)(1)(B).

¹⁷ See *infra* notes 133–209 and accompanying text.

¹⁸ See *infra* notes 21–115 and accompanying text.

¹⁹ See *infra* notes 116–209 and accompanying text.

²⁰ See *infra* notes 210–264 and accompanying text.

²¹ *Regulation of Tobacco Products: Hearings Before the Subcomm. on Health and the Env't of the H. Comm. on Energy and Commerce*, 103d Cong. 527 (1994); William B. Schultz, *The*

was, of course, untrue—“[t]he companies themselves had carefully documented the effects of nicotine on the brain”—but the companies feared that acknowledging nicotine’s addictive effects could subject them to FDA regulation.²²

More than twenty years after this historic hearing, the landscape has shifted dramatically. The addictiveness of nicotine is no longer in dispute, and the FDA now has jurisdiction over tobacco products.²³ But the effects of nicotine are still widely misunderstood,²⁴ and the rise of e-cigarettes, and, more recently, the emergence of synthetic nicotine, continues to present the FDA with challenging legal and regulatory decisions.²⁵

This Part presents the scientific and legal background necessary to explore whether and how the FDA should regulate synthetic nicotine. It starts by examining how nicotine affects the human body²⁶ and how the FDA has regulated (or tried to regulate) tobacco and nicotine.²⁷ It then explores how e-cigarettes fit into the FDA’s regulatory scheme.²⁸ Finally, it discusses how synthetic nicotine threatens to upset the FDA’s efforts to comprehensively regulate nicotine.²⁹

A. Nicotine’s Effects on the Body

Since the 1950s, the major tobacco companies have been aware that nicotine is an addictive substance.³⁰ For instance, in 1963, an internal Brown & Williams report recognized that “nicotine is addictive” and the company was therefore “in the business of selling nicotine, an addictive drug”³¹ Likewise, a 1969 Philip Morris report recognized that “the primary motivation for smoking is to obtain the pharmacological effect of

FDA’s Decision to Regulate Tobacco Products, 18 PACE L. REV. 27, 29 (1997); Philip J. Hilts, *Tobacco Chiefs Say Cigarettes Aren’t Addictive*, N.Y. TIMES, Apr. 15, 1994, at A1.

²² Schultz, *supra* note 21, at 33.

²³ See *infra* notes 53–80 and accompanying text.

²⁴ Jennifer C. Morgan et al., *How People Think About the Chemicals in Cigarette Smoke: A Systematic Review*, 40 J. BEHAVIORAL MED. 553, 557 (2017).

²⁵ See *infra* notes 103–114 and accompanying text.

²⁶ See *infra* notes 30–52 and accompanying text.

²⁷ See *infra* notes 53–80 and accompanying text.

²⁸ See *infra* notes 81–102 and accompanying text.

²⁹ See *infra* notes 103–114 and accompanying texts.

³⁰ *United States v. Philip Morris USA, Inc.*, 449 F. Supp. 2d 1, 515 (D.D.C. 2006), *aff’d*, 566 F.3d 1095 (D.C. Cir. 2009) (“Philip Morris”); Schultz, *supra* note 21, at 33.

³¹ A. YEAMAN, IMPLICATIONS OF BATELLE HIPPO I & II AND THE GRIFFITH FILTER 4 (July 1963), <https://www.industrydocumentslibrary.ucsf.edu/tobacco/docs/hrwh0097> [<https://perma.cc/BW2Q-VJN8>].

nicotine.”³² But motivated in part by fear of FDA regulation, the industry worked to conceal evidence of nicotine’s addictiveness for decades.³³

Despite the industry’s past denials, it is now beyond dispute that “[n]icotine is the drug in tobacco that causes addiction.”³⁴ The physiological mechanisms are complex, but in short, exposure to nicotine activates the nicotine-specific receptors in the brain, and this activation in turn increases levels of dopamine and other neurotransmitters.³⁵ Dopamine provides a pleasurable sensation, and the reinforcing effects of dopamine create and sustain addiction.³⁶ Importantly, the brain adapts to repeated nicotine use, increasing one’s tolerance to it, and that increased tolerance for nicotine is reflected in physiological changes.³⁷ Specifically, chronic nicotine exposure alters the brain’s structure by increasing the number of nicotine-specific receptors.³⁸

Nicotine addiction is characterized by the user’s need to continue dosing, both to maintain the reinforcing effects of nicotine and to reduce the incidence of withdrawal symptoms.³⁹ The reinforcing effects of nicotine on the brain (and other systems) include increased “relaxation, reduced stress, enhanced vigilance, improved cognitive function, mood modulation, and lower body weight.”⁴⁰ Conversely, when withdrawing from nicotine, users experience “nervousness, restlessness, irritability, and anxiety . . .”⁴¹ For regular smokers, the effects of nicotine can wear off quickly; within thirty minutes of smoking, they may already start to feel symptoms of both physical and psychological withdrawal.⁴²

³² See WHY ONE SMOKES 2, 4–11 (1969), <https://www.industrydocumentslibrary.ucsf.edu/tobacco/docs/tjnm0129> [<https://perma.cc/HZ5H-NBV8>].

³³ *Philip Morris*, 449 F. Supp. 2d at 653 (“The Defendants [tobacco industry leaders] have repeatedly made vigorous and impassioned public denials—before Congressional committees, in advertisements in the national print media, and on television—that neither smoking nor nicotine is addictive, and that they do not manipulate, alter, or control the amount of nicotine contained in the cigarettes they manufacture.”).

³⁴ OFFICE ON SMOKING & HEALTH, U.S. DEP’T OF HEALTH & HUMAN SERVS., THE HEALTH CONSEQUENCES OF SMOKING—NICOTINE ADDICTION: A REPORT OF THE SURGEON GENERAL 9 (1988), <https://profiles.nlm.nih.gov/ps/access/NNBBZD.pdf> [<https://perma.cc/LXQ3-RE3N>].

³⁵ OFFICE ON SMOKING & HEALTH, U.S. DEP’T OF HEALTH & HUMAN SERVS., THE HEALTH CONSEQUENCES OF SMOKING—50 YEARS OF PROGRESS: A REPORT OF THE SURGEON GENERAL 113 (2014) [hereinafter 2014 SURGEON GENERAL’S REPORT], <https://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf> [<https://perma.cc/82GF-3TUU>].

³⁶ *Id.* at 113, 785.

³⁷ *Philip Morris*, 449 F. Supp. 2d at 598–99.

³⁸ *Id.*

³⁹ *Id.* at 601; see also 2014 SURGEON GENERAL’S REPORT, *supra* note 35, at 112.

⁴⁰ Neal L. Benowitz, *Pharmacology of Nicotine: Addiction and Therapeutics*, 356 ANN. REV. OF PHARMACOLOGY & TOXICOLOGY 597, 601 (1996).

⁴¹ *Id.*

⁴² *Id.* at 601, 603.

In addition to causing addiction and relieving withdrawal symptoms, nicotine exposure—apart from the risks associated with other components in tobacco—carries its own risks. The World Health Organization has explained that nicotine “can have adverse effects during pregnancy and may contribute to cardiovascular diseases,” and “[a]lthough nicotine itself is not a carcinogen, it may function as a tumour promoter.”⁴³

Moreover, nicotine is particularly harmful for developing brains. For a fetus (exposed through maternal nicotine use), nicotine exposure can cause cellular damage to the brain that is associated with behavioral challenges later in life, including learning disabilities and hyperactivity disorder.⁴⁴ Nicotine also restricts the flow of nutrients and oxygen to the fetal tissues, which is linked to congenital deformities and impaired cardiac development.⁴⁵ For these reasons and others, nicotine is classified as a developmental toxicant by the California Environmental Protection Agency.⁴⁶

Likewise, adolescents—whose brains are not yet fully developed—are particularly vulnerable to nicotine exposure.⁴⁷ Because nicotine exposure at the adolescent age also induces structural changes in the brain, those who begin to use tobacco as adolescents are more likely to smoke into adulthood, have more difficulty quitting, and experience deeper levels of addiction.⁴⁸ Other consequences of early nicotine exposure include changes to the developing limbic system (the emotional core of the brain), which increases the likelihood of developing mood disorders, attention and cognition disorders, and drug-seeking behaviors.⁴⁹

⁴³ World Health Org., Electronic Nicotine Delivery Systems, 3, FCTC/COP/6/10 (July 21, 2014), http://apps.who.int/gb/fctc/pdf/cop6/FCTC_COP6_10-en.pdf [<https://perma.cc/Q9NT-RPJS>] (internal quotation marks omitted).

⁴⁴ 2014 SURGEON GENERAL’S REPORT, *supra* note 35, at 119, 121 (citing Theodore A. Slotkin, *Fetal Nicotine or Cocaine Exposure: Which One Is Worse?*, 285 J. PHARMACOLOGY & EXPERIMENTAL THERAPEUTICS 931 (1998)).

⁴⁵ See Donna S. Lambers & Kenneth E. Clark, *The Maternal and Fetal Physiologic Effects of Nicotine*, 20 SEMINARS PERINATOLOGY 115, 115 (1996).

⁴⁶ 2014 SURGEON GENERAL’S REPORT, *supra* note 35, at 471.

⁴⁷ Neuroscience research over the past few decades has shown, contrary to earlier assumptions, that brain development continues into one’s twenties. See ELIZABETH S. SCOTT & LAURENCE STEINBERG, *RETHINKING JUVENILE JUSTICE* 44 (2010) (“Scientists have found clear evidence that the brain continues to mature through adolescence and into the early twenties, with large-scale structural change taking place during this period.”).

⁴⁸ OFFICE ON SMOKING & HEALTH, U.S. DEP’T OF HEALTH & HUMAN SERVS., *E-CIGARETTE USE AMONG YOUTH AND YOUNG ADULTS: A REPORT OF THE SURGEON GENERAL 105* (2016) [hereinafter 2016 SURGEON GENERAL’S REPORT], https://e-cigarettes.surgeongeneral.gov/documents/2016_SGR_Full_Report_non-508.pdf [<https://perma.cc/9LKT-9H4L>].

⁴⁹ Eric R. Kandel & Denise B. Kandel, *A Molecular Basis for Nicotine as a Gateway Drug*, 371 NEW ENG. J. MED. 932, 941–42 (2014); Menglu Yuan et al., *Nicotine and the Adolescent Brain*, 593 J. PHYSIOLOGY 3397, 3397 (2015).

Although the effects outlined above raise public health concerns, nicotine itself—separate and apart from tobacco use—may hold promise as a treatment for certain medical conditions. For instance, there is some preliminary evidence—albeit sometimes funded or conducted by the tobacco industry⁵⁰—that nicotine could be used to treat the symptoms of Alzheimer’s disease, Parkinson’s disease, Schizophrenia, and other illnesses.⁵¹

In short, although nicotine is not the primary lethal component of tobacco products, it is well known that nicotine use causes addiction as well as other negative public health consequences.⁵² For purposes of FDA regulation, it is notable that it does so by inducing permanent physiological changes in the brain. Nicotine, isolated from tobacco, may also hold some public health promise. Of course, if a nicotine-containing product were marketed as a treatment for a disease or its symptoms, there is no question that the FDA would consider it a drug.

B. The FDA’s History of Using Its Drug-Related Authority to Regulate Tobacco and Nicotine

The FDA oversees drugs throughout their lifecycle, from the start of research through their use in clinical care. A critical component of the FDA’s regulation of drugs is the agency’s gatekeeping function. A new drug cannot be marketed in the United States unless the FDA determines it is safe and effective for its proposed use.⁵³

What constitutes a *drug* subject to the FDA’s authority? The FDCA defines a “drug” as an “article” that is “intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease” or that is “intended to affect

⁵⁰ Janine K. Cataldo et al., *Cigarette Smoking Is a Risk Factor for Alzheimer’s Disease: An Analysis Controlling for Tobacco Industry Affiliation*, 2010 J. ALZHEIMER’S DISEASE 465, 465–80 (finding that studies funded by the tobacco industry reported that smoking was protective against Alzheimer’s disease, whereas studies without industry funding found that smoking increased the risk of Alzheimer’s disease or that there was no clear association); cf. 2014 SURGEON GENERAL’S REPORT, *supra* note 35, at 123 (“Nonindustry-funded authors reported both positive and negative findings [on the relationship between nicotine and cognitive performance], while industry-funded authors reported positive findings almost exclusively.”).

⁵¹ 2014 SURGEON GENERAL’S REPORT, *supra* note 35, at 123; see also Benowitz, *supra* note 40, at 607.

⁵² See *supra* notes 39–49 and accompanying text.

⁵³ 21 U.S.C. §§ 331(d), 355(a)–(d) (2012). “New drugs,” as defined by the FDCA, are those drugs that are not generally recognized as safe and effective, or have not been marketed for a material time and to a material extent. *Id.* § 321(p). The overwhelming majority of prescription drugs, and many over-the-counter drugs introduced into the market after 1972, are new drugs. See U.S. FOOD & DRUG ADMIN., MARKETING UNAPPROVED DRUGS—COMPLIANCE POLICY GUIDE 12 (Sept. 2011), <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070290.pdf> [<https://perma.cc/RET7-QSEV>].

the structure or any function of the body”⁵⁴ Therefore, the “intended use” of a product—determined by the “objective intent of the persons legally responsible for the labeling”⁵⁵—is the key to determining whether a product is a drug within the FDA’s jurisdiction.⁵⁶ Although the FDA has applied commonsense limits to its interpretation of what falls within the drug definition, the definition is quite broad.⁵⁷ It captures products that are commonly understood to be drugs—such as cancer therapies—as well as products that a lay person or healthcare provider may not intuitively consider to be drugs—such as antiperspirant, which is intended to inhibit the body’s sweat function.⁵⁸ As the Supreme Court has explained, the FDCA “define[s] ‘drug’ far more broadly than does the medical profession.”⁵⁹

⁵⁴ 21 U.S.C. § 321(g)(1).

⁵⁵ 21 C.F.R. § 201.128 (2017); *see also id.* § 801.4 (providing the same definition for intended use of devices). The FDA made certain controversial changes to the regulatory definition of intended use in 2017. As of the time of writing, the FDA has indefinitely delayed the effective date for the contested changes to “allow further consideration.” The agency, however, did not change, nor has the industry objected to, this aspect of the definition. Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding “Intended Uses”; Partial Delay of Effective Date, 83 Fed. Reg. 11,639, 11,639 (Mar. 16, 2018) [hereinafter 2018 FDA Clarification]; Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products, 82 Fed. Reg. 14,320, 14,320–24 (Mar. 20, 2017); Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding “Intended Uses,” 82 Fed. Reg. 2193, 2198, 2200 (Jan. 9, 2017) [hereinafter January 2017 FDA Clarification].

⁵⁶ The FDA’s jurisdiction and enforcement authority is also generally linked to a drug’s movement (or its components’ movement) in interstate commerce. *See* 21 U.S.C. § 331; Patricia J. Zettler, *Pharmaceutical Federalism*, 92 IND. L.J. 845, 879–80 (2017). Given modern production processes that typically involve at least components crossing state or national borders, and finished products crossing state and national boundaries to reach customers, this limitation on FDA authority is unlikely to be relevant to nicotine products.

⁵⁷ For example, the FDA has explained that, although whole organs intended for transplant “fall within the literal language” of the drug definition, the agency does not intend to regulate them as drugs for various reasons. *Statement by the Food and Drug Administration Concerning Its Legal Authority to Regulate Human Organ Transplants and to Prohibit Their Sale: Hearing Before the Subcomm. on Investigations and Oversight, H. Comm. on Sci. & Tech.*, 98th Cong. (1983), reprinted in PETER HUTT ET AL., *FOOD AND DRUG LAW: CASES AND MATERIALS* 939–41 (2013). Likewise, in the device context where the FDA’s jurisdiction also largely depends on a product’s intended use, the FDA has applied commonsense limitations to its jurisdiction by, for instance, declining to construe all exercise equipment—which, of course, is intended to affect the structure or function of the body—to be devices. *See, e.g.*, 21 C.F.R. § 890.5350 (2017); *see also* Physical Medicine Devices, 48 Fed. Reg. 53,032, 53,035 (Nov. 23, 1983) (“FDA has changed the regulations classifying many physical medicine devices to clarify that the regulations apply only to those products intended for medical purposes.”).

⁵⁸ *See* PETER HUTT ET AL., *supra* note 57, at 117.

⁵⁹ *United States v. Bacto-Unidisk*, 394 U.S. 784, 793 (1969).

Since at least 1984, the FDA has regulated nicotine-containing products intended to assist with smoking cessation as drugs.⁶⁰ Because of the strong causal link between smoking and numerous diseases, the FDA considers sellers' claims that a product aids in smoking cessation to be evidence that the product is "intended for use in the . . . mitigation, treatment, or prevention of disease"⁶¹ Thus, smoking cessation products such as nicotine-containing gums, lozenges, and transdermal patches (collectively referred to as Nicotine Replacement Therapies, or "NRT") are regulated as drugs and require FDA approval before they can be sold.⁶²

If nicotine is a drug for purposes of NRT, is it also a drug when used in tobacco products themselves? The FDA raised this question in 1996, when it tried to regulate tobacco products as drug-device combination products.

1. The 1996 Rule: The FDA's First Attempt to Regulate Tobacco Products

In 1996, the FDA tried—ultimately unsuccessfully—to argue that because nicotine was a drug "intended to affect the structure or any function of the body," it could regulate tobacco products such as cigarettes and smokeless tobacco as drug-delivery devices.⁶³ To support this assertion, the agency pointed to several categories of evidence: tobacco products do, in fact, affect the structure and function of the body in myriad ways; a reasonable tobacco seller would foresee that consumers will use tobacco products to obtain the biological effects of nicotine; and consumers do predominantly use tobacco products for their biological effects.⁶⁴ The FDA also relied heavily on what was then recently discovered evidence that the tobacco companies knew that nicotine was addictive (despite their public denials) and deliberately manipulated nicotine levels in tobacco products in order to

⁶⁰ *Drugs@FDA: FDA Approved Drug Products*, FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=018612> [<https://perma.cc/SQ2U-HLGX>].

⁶¹ January 2017 FDA Clarification, *supra* note 55, at 2194, 2198, 2214.

⁶² See 21 C.F.R. § 310.544. Notably, NRT products are designed to treat tobacco addiction without inducing sustained, long-term use. NRTs have been criticized as being unappealing to current smokers precisely because they have been calibrated not to create dependence. Brent Caldwell et al., *A Systematic Review of Nicotine by Inhalation: Is There a Role for the Inhaled Route?*, 14 NICOTINE & TOBACCO RES. 1127, 1127 (2012). As of the time of writing, the FDA is considering how NRT products, and the agency's regulation of NRT products, could be improved. See The Food and Drug Administration's Approach to Evaluating Nicotine Replacement Therapies; Public Hearing; Request for Comments, 82 Fed. Reg. 56,759, 56,759 (Nov. 30, 2017).

⁶³ See generally DAVID KESSLER, A QUESTION OF INTENT: A GREAT AMERICAN BATTLE WITH A DEADLY INDUSTRY (2001) (examining in detail the FDA's attempt to regulate tobacco products).

⁶⁴ See *id.*

create and sustain addiction.⁶⁵ This new evidence, in the FDA's view, justified the reversal of its prior position that tobacco products did not qualify as drugs under the FDCA.⁶⁶

Immediately after the FDA asserted jurisdiction over tobacco products, the major tobacco companies filed suit.⁶⁷ After four years of litigation, in 2000, a 5–4 majority of the Supreme Court ruled in *FDA v. Brown & Williamson* that the FDA lacked the authority to regulate tobacco products as drugs or devices when those tobacco products are “customarily marketed . . . without . . . claims of therapeutic benefit.”⁶⁸ To reach this conclusion, the Court pointed to the FDCA’s “core objective” of ensuring that drugs and devices are safe and effective for their intended use.⁶⁹ Without disagreeing that nicotine-containing tobacco products were “intended to affect the structure or any function of the body,” the majority concluded that such products could not be regulated as drugs or devices because tobacco products could never meet the “safe and effective” standard.⁷⁰ The FDA, in the majority’s view, would therefore be required to ban the sale of tobacco products if they came under the agency’s jurisdiction.⁷¹

The majority’s opinion also rested heavily on tobacco’s “unique place in American history and society.”⁷² Referring to the economic, social, and political significance of the tobacco industry—which it described as “one of the greatest basic industries of the United States”—the majority concluded that “Congress could not have intended to delegate a decision of such economic and political significance to [the FDA] in so cryptic a fashion.” As a result of the Supreme Court’s decision, the FDA was left without the authority to regulate tobacco products “as customarily marketed” absent more explicit authorization from Congress, although it could still regulate other nicotine-containing products, such as NRTs, as drugs.

⁶⁵ *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 172 (2000) (Breyer, J., dissenting). In 1994, Congress held hearings, known as the Waxman Hearings, to investigate the health harms created by tobacco. At those hearings, the seven CEOs of the major tobacco companies of the time denied that nicotine was addictive and maintained that their manipulation of nicotine levels in products was an effort to enhance flavor, not sustain addiction. Hiltz, *supra* note 21, at A20.

⁶⁶ *Brown & Williamson*, 529 U.S. at 126–29 (majority opinion).

⁶⁷ *Id.* at 129.

⁶⁸ *Id.* at 127.

⁶⁹ *Id.* at 142.

⁷⁰ *Id.* at 132–33, 161.

⁷¹ *Id.* at 161. As the dissent noted, the FDA had interpreted the FDCA differently than the majority did, concluding that the law gave the FDA the flexibility to regulate tobacco products without banning them. *Id.* at 181 (Breyer, J., dissenting). The regulation it proposed would have limited the marketing and sales of tobacco products, but would not have banned them. *Id.* at 174.

⁷² *Brown & Williamson*, 529 U.S. at 159 (majority opinion).

2. The Tobacco Control Act

Nine years after the *Brown & Williamson* decision, Congress passed—and President Obama signed—the TCA, granting the FDA broad jurisdiction over tobacco products.⁷³ Under the TCA, tobacco products are now a separate regulatory category distinct from drugs and devices.⁷⁴ Instead of asking the FDA to assure that tobacco products are “safe and effective”—which, as the majority in *Brown & Williamson* noted, may be inappropriate for an inherently deadly product—the TCA requires the FDA to regulate tobacco products based on a population-level public health standard.⁷⁵ Under this standard, the FDA must determine that its regulations are “appropriate for the protection of the public health” after considering “the risks and benefits to the population as a whole, including users and nonusers of the tobacco product.”⁷⁶

The TCA was a negotiated compromise between the tobacco industry and the public health community.⁷⁷ The key compromise at its core is tobacco products that were already on the market would be “grandfathered,” but any *new* tobacco products must demonstrate either that they are “substantially equivalent” to grandfathered products or that allowing their sale would be “appropriate for the protection of public health.”⁷⁸ This compromise allowed the tobacco industry to keep selling tobacco products, while (at least in theory) ensuring that newly introduced products would benefit, and not harm, public health.

In addition to the premarket review requirements, the TCA also gave the FDA broad authority over other areas of tobacco regulation including health claims, sales and marketing restrictions, and “product standards,” including mandated reductions in nicotine levels.⁷⁹ Although a full review of the TCA’s provisions is beyond the scope of this Article, the law gives the FDA extremely powerful regulatory tools to reduce the death and disease caused by tobacco use.⁸⁰

⁷³ See Family Smoking Prevention and Tobacco Control Act, 123 Stat. 1776, 1783–842 (2009) (granting FDA more extensive jurisdiction over tobacco products).

⁷⁴ *Id.* at 1842–49.

⁷⁵ See *id.* at 1796.

⁷⁶ *Id.* § 906(d)(1), 123 Stat. at 1796.

⁷⁷ Desmond Jenson et al., *FDA’s Misplaced Priorities: Premarket Review Under the Family Smoking Prevention and Tobacco Control Act*, 25 TOBACCO CONTROL 246, 246 (2016).

⁷⁸ Family Smoking Prevention and Tobacco Control Act § 910, 123 Stat. at 1807; see also Jenson et al., *supra* note 77, at 246.

⁷⁹ Family Smoking Prevention and Tobacco Control Act, 123 Stat. at 1842–49. These restrictions can be applied to grandfathered products.

⁸⁰ For a detailed description of the TCA’s provisions, see generally Corinne G. Husten & Lawrence R. Deyton, *Understanding the Tobacco Control Act: Efforts by the US Food and Drug*

C. The Rise of E-cigarettes

The requirements of the TCA applied immediately to certain enumerated tobacco products: cigarettes, smokeless tobacco, and roll-your-own tobacco.⁸¹ The law, however, did not immediately extend the FDA's authority to other types of tobacco products, including e-cigarettes, hookah tobacco, cigars, cigarillos, and pipe tobacco.⁸² Instead, the TCA provided that the FDA could make these products, and any other product meeting the statutory definition of a "tobacco product," subject to the law's requirements by promulgating a regulation.⁸³

Consistent with the process outlined in the TCA, in May 2016, the FDA finalized a rule doing just that—the Deeming Rule. The rule deems any product meeting the statutory definition of a "tobacco product,"⁸⁴ including e-cigarettes, to be subject to the agency's tobacco regulatory scheme, including the pre-market review requirements outlined above.⁸⁵ Tobacco products brought within the scope of the FDA's authority by the Deeming Rule will also now include warning labels and comply with various other restrictions, including a prohibition on false or misleading claims.⁸⁶

The rapid emergence of e-cigarettes was one of the forces driving the FDA to issue the Deeming Rule. Unlike combustible cigarettes, e-cigarettes deliver nicotine by heating (not burning) a nicotine-containing liquid until it

Administration to Make Tobacco-Related Morbidity and Mortality Part of the USA's Past, Not Its Future, 381 LANCET 1570 (2013).

⁸¹ 21 U.S.C. § 387a(b) (2012).

⁸² *See id.*

⁸³ *Id.*

⁸⁴ Deeming Rule, 81 Fed. Reg. 28,974, 29,102 (May 10, 2016). The Deeming Rule also includes components and parts, which means "any software or assembly of materials intended or reasonably expected: (1) [t]o alter or affect the tobacco product's performance, composition, constituents or characteristics; or (2) to be used with or for the human consumption of a tobacco product." *Id.* at 29,015.

⁸⁵ *Id.* at 28,977. This premarket review process will undoubtedly be much harder for e-cigarette companies because of the amount of data and capital it takes to put forth a new product application. The FDA, however, delayed the deadline for these new product applications. *FDA Comprehensive Plan*, *supra* note 1. Notably, several public health groups have challenged the agency's delay in regulation. *See, e.g., Am. Acad. of Pediatrics v. FDA*, No. 8:18-cv-883 (D. Md. filed Mar. 27, 2018).

⁸⁶ Deeming Rule, Fed. Red. at 28,975–76. Newly deemed tobacco products may not yet be following some of these requirements. This is because the FDA has specified different dates at which it will enforce compliance with the various requirements of the Deeming Rule, many of which post-date the writing of this Article. *See* U.S. FOOD & DRUG ADMIN., CTP-68-RB, EFFECTIVE AND COMPLIANCE DATES APPLICABLE TO RETAILERS, MANUFACTURERS, IMPORTERS, AND DISTRIBUTORS OF NEWLY DEEMED TOBACCO PRODUCTS 1–7 (2017), <https://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM501016.pdf> [<https://perma.cc/2E6L-2FWL>].

aerosolizes, which the user then inhales, referred to as *vaping*.⁸⁷ The liquid, referred to as an “e-liquid,” usually contains nicotine derived from tobacco, a humectant (propylene glycol and/or vegetable glycerin), and flavorings.⁸⁸ First introduced in the United States in 2007, e-cigarette use has risen exponentially. By 2014, almost half (forty-nine percent) of daily smokers reported ever having used e-cigarettes,⁸⁹ and e-cigarette use is now more common than cigarette use among high school and middle school students.⁹⁰

As a matter of public health, e-cigarettes hold both promise and peril.⁹¹ Although the long-term health effects of e-cigarettes are unknown, they are likely far less lethal than cigarettes and other combustible products.⁹² If current smokers switched completely from smoking to e-cigarette use that would likely produce enormous public health gains. Currently, however, the

⁸⁷ Early e-cigarettes were called “cigalikes” and mimicked the size, shape, and design of cigarettes. These products have evolved over time and now many do not resemble cigarettes at all; some of the most popular systems include detachable parts that allow the user to customize the vaping experience, including the voltage, the temperature, the size of the tank, etc., and allow for the mixing and switching of new flavors easily. At least some of the newer products appear to be more efficient at delivering nicotine. *Vaporizers, E-Cigarettes, and Other Electronic Nicotine Delivery Systems (ENDS)*, FOOD & DRUG ADMIN. (Mar. 20, 2018), <https://www.fda.gov/tobacco-products/labeling/productsingredientscomponents/ucm456610.htm> [<https://perma.cc/ZPH7-SGZW>].

⁸⁸ *Id.*

⁸⁹ Cristine D. Delnevo et al., *Patterns of Electronic Cigarette Use Among Adults in the United States*, 18 NICOTINE & TOBACCO RES. 715, 716 (2016).

⁹⁰ Ahmed Jamal et al., *Tobacco Use Among Middle and High School Students—United States, 2011–2016*, 66 MORBIDITY & MORTALITY WKLY. REP. 597, 597 (2017).

⁹¹ See NAT’L ACADS. OF SCI., ENG’G, MED., PUBLIC HEALTH CONSEQUENCES OF E-CIGARETTES 15-16 (2018) (conducting a comprehensive review of the scientific literature on e-cigarettes and concluding that e-cigarettes “contain fewer toxicants” than conventional cigarettes and “might be useful as a cessation aid in smokers who use e-cigarettes exclusively,” but that the long-term health effects of e-cigarettes are unknown and that “youth who begin with e-cigarettes are more likely to transition to combustible tobacco cigarette use”). Although not addressed in this Article, the National Academies committee report noted that secondhand exposure to e-cigarette aerosols may also raise health concerns. *Id.* at 77–84. The committee found “conclusive evidence that e-cigarette use increases airborne concentrations of particulate matter and nicotine in indoor environments compared with background levels,” but it cautioned that due to the limited amount of research on this subject, “it is unclear how detrimental exposure to second-hand e-cigarette emissions is to the non-user.” *Id.* at 4, 17, 84, 410.

⁹² Although the harms of e-cigarettes are likely less than combustible products, there is still potential for significant harms from the products, the nicotine, the flavorings, or the components or parts used to vaporize the liquid. For example, at least one experiment has found that use of e-cigarettes can lead to the stiffening of blood vessels, similar to what smoking combustible cigarettes does, in ways that may raise the likelihood of cardiovascular events. See Charalambos Vlachopoulos et al., *Electronic Cigarette Smoking Increases Aortic Stiffness and Blood Pressure in Young Smokers*, 67 J. AM. C. CARDIOLOGY 2082, 2082 (2016); Roberto Carnevale et al., *Acute Impact of Tobacco vs Electronic Cigarette Smoking on Oxidative Stress and Vascular Function*, 150 CHEST 606, 606 (2016).

majority of people who use e-cigarettes are *also* smoking.⁹³ Youth e-cigarette use is additionally a concern, both because of the effects of nicotine on the developing brain,⁹⁴ and because of accumulating evidence that e-cigarette use is a gateway to smoking.⁹⁵ Moreover, the history of tobacco product marketing suggests that the industry has economic incentives to target the youth population in its marketing, and is likely to do so.⁹⁶

Although not explicitly stated, the FDA's new "comprehensive plan" is built on the assumption that if the nicotine in cigarettes is reduced to non-addictive or minimally addictive levels, many current smokers will transition to e-cigarettes as the best available substitute. For this reason, the FDA's plan seeks to encourage "innovations" in the e-cigarette market and delays the effective date for some of the Deeming Rule's more costly requirements.⁹⁷ At the same time, the FDA recognizes that e-cigarettes cannot be completely unregulated. The Deeming Rule already prohibits unsubstantiated health claims, bars sales to minors, and requires e-cigarette companies to disclose

⁹³ Charlotte A. Schoenborn, *QuickStats: Cigarette Smoking Status Among Current Adult E-cigarette Users, by Age Group—National Health Interview Survey, United States, 2015*, 65 MORBIDITY & MORTALITY WKLY. REP. 1177, 1177 (2016).

⁹⁴ See *supra* notes 44–49 and accompanying text.

⁹⁵ See Jessica Barrington-Trimis et al., *E-cigarettes and Future Cigarette Use*, 138 PEDIATRICS 1, 1 (2016); Adam M. Leventhal et al., *Association of Electronic Cigarette Use with Initiation of Combustible Tobacco Product Smoking in Early Adolescence*, 314 JAMA 700, 700 (2015); Brian A. Primack et al., *Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults*, 169 JAMA PEDIATRICS 1018, 1022 (2015) (suggesting that "[b]ecause e-cigarettes deliver nicotine more slowly than traditional cigarettes, they may serve as a 'nicotine starter,' allowing a new user to advance to cigarette smoking as he or she becomes tolerant of the initial adverse effects"). These findings include suggestive evidence that some youth who would not otherwise be likely to become smokers progress to smoking after e-cigarette use. Barrington-Trimis et al., *supra*, at 1; Leventhal et al., *supra*, at 700; Primack et al., *supra*, at 1022. Also, one should note that the history of tobacco marketing suggests that e-cigarette companies, despite statements to the contrary, have strong economic incentives to sell to youth. Ross Hammond, WHO, *Tobacco Advertising & Promotion: The Need for a Coordinated Global Response*, 9 (2000).

⁹⁶ See generally CAMPAIGN FOR TOBACCO-FREE KIDS: TOBACCO COMPANY MARKETING TO KIDS (Apr. 2018), <https://www.tobaccofreekids.org/assets/factsheets/0008.pdf> [<https://perma.cc/XA87-KV28>] (providing a compilation of Tobacco Industry statements, actions, and quotations regarding targeted marketing of children).

⁹⁷ *FDA Comprehensive Plan*, *supra* note 1. Although it is beyond the scope of this Article, there is room to question whether the FDA's approach is well designed to encourage innovation. The extended dates for premarket review apply only to products that were on the market as of August 8, 2016. *Id.* After that date, any new product cannot be sold until it undergoes premarket review by the FDA. Thus, the extended dates provide a reprieve to e-cigarette companies that were worried they would be unable to comply with the FDA's requirements—but does nothing to encourage companies to create new, innovative products that meet the FDA's requirements or improve on existing products. See *id.*

their ingredient lists to the FDA; the FDA has pledged to go further and develop product standards relating to battery safety and child-proofing.⁹⁸

Regardless of where one stands on the harm reduction debate surrounding e-cigarettes, all sides should be able to agree that there is a role for reasonable regulation (although there may be disagreement over the extent of regulation that is *reasonable*). A complete lack of regulation invites problems that have already been observed in the, until recently, unregulated e-cigarette market: “false and misleading claims,”⁹⁹ inaccurate labeling,¹⁰⁰ dangerously shoddy product quality,¹⁰¹ unabashed marketing to youth,¹⁰² and more. Nevertheless, even with full implementation of the Deeming Rule, it appears as though one portion of the e-cigarette market may remain completely unregulated, at least for now: synthetic nicotine products.

D. The Emergence of Synthetic Nicotine

The Deeming Rule generally applies to e-cigarettes that contain nicotine “made or derived from tobacco”¹⁰³ In the last few years, however, over a dozen e-cigarette brands have begun to sell products containing syn-

⁹⁸ *Id.* The FDA also states that it intends to propose a rule for the regulation of flavors in newly deemed products. *Id.*

⁹⁹ See Elizabeth Klein et al., *Online E-cigarette Marketing Claims: A Systematic Content and Legal Analysis*, 2 TOBACCO REGULATORY SCI. 252, 262 (2016).

¹⁰⁰ See Kelly Buettner-Schmidt et al., *Electronic Cigarette Refill Liquids: Child-Resistant Packaging, Nicotine Content, and Sales to Minors*, 31 J. PEDIATRIC NURSING 373, 373 (2016).

¹⁰¹ See Jamie Harshman et al., *Burns Associated with E-cigarette Batteries: A Case Series and Literature Review*, 19 CAN. J. EMERGENCY MED. 1, 1 (2017), https://www-cambridge-org.proxy.bc.edu/core/services/aop-cambridge-core/content/view/7ED4071739CCAA5CA071BB88EA3C27FC/S148180351700032Xa.pdf/burns_associated_with_ecigarette_batteries_a_case_series_and_literature_review.pdf [<https://perma.cc/B7LJ-WWU9>].

¹⁰² See generally Jennifer C. Duke et al., *Exposure to Electronic Cigarette Television Advertisements Among Youth and Young Adults*, 134 PEDIATRICS 1 (2014).

¹⁰³ Deeming Rule, 81 Fed. Reg. 28,974, 28,976 (May 10, 2016). As of the time of writing, the FDA has identified three circumstances where non-nicotine e-liquids or e-cigarettes are still subject to FDA authority, noting that:

e-liquids marketed as “nicotine-free” may properly be considered tobacco products—or components or parts thereof—under certain circumstances. As the record demonstrates, some e-liquids claiming to be nicotine-free actually contain[] high levels of nicotine Others are tobacco flavored, and are thus made or derived from tobacco regardless of their nicotine content And nicotine-free e-liquids are sometimes mixed with liquid nicotine before inhalation, . . . affecting not only the composition of the substance ultimately vaporized, but also its constituents and characteristics

thetic nicotine, developed in a lab without the use of tobacco plants.¹⁰⁴ This product is chemically identical to the nicotine found in tobacco plants—and similarly addictive—but likely falls outside of the FDA’s tobacco-related authority.

Sellers of synthetic nicotine products claim they are an important innovation in nicotine products, because tobacco-derived nicotine inevitably contains some contaminants—including potentially carcinogenic ones—from tobacco plants, whereas synthetic nicotine is *pure*.¹⁰⁵ For the same reason, sellers contend that synthetic nicotine products offer a “comparatively clean flavor” when used in e-liquids.¹⁰⁶

Although the technology to create synthetic nicotine has existed since the 1940s, the high cost of production has limited its commercial use in products intended for human consumption.¹⁰⁷ Now, however, more efficient production methods seem to have been developed, and some companies are selling synthetic nicotine products (or, at least, products that sellers claim contain synthetic nicotine) at prices comparable to other e-liquids.¹⁰⁸ For example, we observed that one company sells 60 mL of its “mangolito” flavor e-juice with tobacco-derived nicotine for \$24.99, and it sells the same amount of the same flavor e-juice with synthetic nicotine for \$27.99.¹⁰⁹ Moreover, although the market for products containing synthetic nicotine currently appears to be dominated by e-liquids, synthetic nicotine could be used as an ingredient in any product in which a seller wants to include nicotine. For example, one seller has announced plans to launch a gum that contains synthetic nicotine, and before the TCA was enacted, companies (unsuccessfully) attempted to market water that contained tobacco-derived nicotine as a dietary supplement.¹¹⁰

¹⁰⁴ Sarah Zhang, *E-Cigs Are Going Tobacco-Free with Synthetic Nicotine*, WIRED (June 27, 2016, 7:00 AM), <https://www.wired.com/2016/06/vaping-industry-wants-go-post-tobacco-synthetic-nicotine/> [https://perma.cc/V22S-ZY82].

¹⁰⁵ See, e.g., *Zia Gum*, NEXTGENERATION LABS (2018), <http://www.nextgenerationlabs.com/zia-gum/> [https://perma.cc/4NHB-BWC8].

¹⁰⁶ See Zhang, *supra* note 104.

¹⁰⁷ 2016 SURGEON GENERAL’S REPORT, *supra* note 48, at 17.

¹⁰⁸ Although at least one seller has been awarded a patent on its process for producing synthetic nicotine, to the best of the author’s knowledge, no third parties have confirmed that the nicotine that sellers market as synthetic is, in fact, synthesized in a lab and not derived from tobacco. For the purposes of this Article, however, we assume that products marketed as containing synthetic nicotine do contain it. See e.g., U.S. Patent No. 9,556,142 (filed Oct. 22, 2015).

¹⁰⁹ *Mangolito Premium E-Liquid*, EJUICE, <https://www.ejuices.com/products/mangolito?variant=25544343112> [https://perma.cc/UGQ6-DZF7]; see also *Mangolito TFN Premium E-Liquid*, EJUICE, <https://www.ejuices.com/products/mangolito-tfn?variant=27307416072> [https://perma.cc/TVP5-DSAV].

¹¹⁰ See, e.g., *Center for Drug Evaluation and Research 2002*, FOOD & DRUG ADMIN. (updated May 2, 2016), <https://wayback.archive-it.org/7993/20170723183304/https://www.fda.gov/ICECI/>

One company asked the FDA for clarification on whether synthetic nicotine products would fall within the Deeming Rule's scope.¹¹¹ Although the FDA explained that synthetic nicotine products must be evaluated on a "case-by-case basis," it also acknowledged that "it's possible [such products] would not be regulated by the FDA as . . . tobacco product[s]."¹¹² Indeed, we think it likely that e-cigarettes and other products that use only synthetic nicotine—which, by definition, is not "made or derived from tobacco"—are not tobacco products under the TCA.¹¹³ Thus, these products are not subject to any of the Deeming Rule's regulations—no premarket approval requirements, no warning labels, no prohibition on health-related claims, and so forth. This regulatory gap is problematic.¹¹⁴ As discussed in the following Part, however, the FDA has a viable option for closing it: classifying synthetic nicotine products as drugs.¹¹⁵

II. THE LEGAL CASE FOR REGULATING SYNTHETIC NICOTINE PRODUCTS AS DRUGS

Some in the e-cigarette industry have claimed synthetic nicotine products' escape from the requirements of the Deeming Rule and the FDA's tobacco regulatory scheme as a "victory," seemingly concluding that if synthetic nicotine products are not tobacco products, they are not subject to any FDA regulation.¹¹⁶ The question of whether synthetic nicotine products are tobacco products, however, is not the end of the inquiry into the FDA's jurisdiction. This Part argues that examining the relevant statutory provisions, case law, and regulations, as well as other agency interpretations of the law,

EnforcementActions/EnforcementStory/EnforcementStoryArchive/ucm103554.htm [https://perma.cc/6HSW-AUBJ]; *Zia Gum*, *supra* note 105. Nicotine-containing products cannot be dietary supplements under the FDCA. *See infra* note 126 and accompanying text.

¹¹¹ *Commonly Asked Questions*, *supra* note 14.

¹¹² *Id.*

¹¹³ 21 U.S.C. § 321(rr)(1) (2012).

¹¹⁴ Though not addressed in this Article, one important concern is that if the FDA proceeds with mandating reductions in nicotine levels in cigarettes and synthetic nicotine products remain unregulated, a market could develop for synthetic nicotine liquid that consumers could add into their low-nicotine cigarettes. This could undermine the effectiveness of an FDA policy intended to render cigarettes non-addictive. *See* Dorothy K. Hatsukami et al., *Nicotine Reduction: Strategic Research Plan*, 15 NICOTINE & TOBACCO RES. 1003, 1010 (2013) (noting that consumers' post-market addition of nicotine back into the product could be an "unintended consequence" of a nicotine reduction regulation).

¹¹⁵ *See infra* notes 116–209 and accompanying text.

¹¹⁶ Tony Ottomanelli II, *Update: Nicopure v. FDA Lawsuit*, VAPING POST (Dec. 20, 2016), <http://www.vapingpost.com/2016/12/20/update-nicopure-v-fda-lawsuit/> [https://perma.cc/2K6A-9WRR].

reveals that synthetic nicotine products should be considered to be drugs under the FDCA.¹¹⁷

A. The Flexibility to Regulate Synthetic Nicotine Products as Drugs

The FDCA defines a “drug” as an “article” “intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease” or “intended to affect the structure or any function of the body”¹¹⁸ Although courts (and the FDA) have generally construed this definition quite broadly, the definition does not cover “customarily marketed” tobacco products.¹¹⁹ As previously discussed in Part I,¹²⁰ in *FDA v. Brown & Williamson*, a majority of the Supreme Court concluded that—before the enactment of the TCA—Congress had “clearly precluded the FDA from asserting jurisdiction to regulate tobacco products as drugs or devices when those tobacco products were customarily marketed . . . without . . . claims of therapeutic benefit.”¹²¹

Courts have continued to take this position after the TCA’s enactment. In 2010, in *Sottera v. FDA*, an e-cigarette company sued the FDA after the agency sought to regulate the company’s products as drug-device combinations.¹²² Relying on *Brown & Williamson*, the D.C. Circuit concluded that, because the e-cigarettes at issue had tobacco-derived nicotine and therefore met the TCA’s definition of a “tobacco product,” the FDA *must* regulate

¹¹⁷ See 21 U.S.C. § 321(g)(1). Depending on how a synthetic nicotine product is marketed—for example, either as a liquid alone or as a liquid combined with a mechanism for delivery—it might be categorized as either a drug or a drug-device combination product. This Article, however, generally describes synthetic nicotine products as drugs. Even if a given synthetic nicotine product is a drug-device combination product, the FDA would likely regulate the product as a drug. This is because, for combination products, the FDA must determine the product’s “primary mode of action”—that is, the component that “provides the most important therapeutic action”—and oversee the product accordingly. *Id.* § 353(g); 21 C.F.R. § 3.2 (2017). For synthetic nicotine products, it is the nicotine liquid that creates an effect in the body, and any device component is intended solely to deliver the nicotine. Therefore, as with drug-device combination products like prefilled syringes, the FDA is likely to regulate combination synthetic nicotine products as drugs. Additionally, the relevant language in the definitions of “drug” and “device” in the FDCA are nearly identical. Both focus on whether an “article” is “intended for use” in diagnosing, curing, mitigating, treating, or preventing disease, or is “intended to affect the structure or any function of the body” 21 U.S.C. § 321(g)(1), (h). Thus, FDA jurisdiction over synthetic nicotine products, and many relevant requirements that come with such jurisdiction, do not turn on whether a given product would be regulated as a drug or drug-device combination.

¹¹⁸ 21 U.S.C. § 321(g)(1).

¹¹⁹ See *Sottera, Inc. v. FDA*, 627 F.3d 891, 894 (D.C. Cir. 2010) (citing *FDA v. Brown & Williamson Tobacco, Inc.*, 529 U.S. 120, 126, 159 (2000)).

¹²⁰ See *supra* notes 21–114 and accompanying texts.

¹²¹ *Brown & Williamson*, 529 U.S. at 126.

¹²² *Sottera*, 627 F.3d at 893.

them as tobacco products, so long as they are “customarily marketed.”¹²³ That is, according to *Sottera*, the FDA lacked the discretion to regulate the e-cigarettes pursuant to its drug and device authorities, provided that the seller was not making “therapeutic claims.”¹²⁴

Consistent with *Sottera*, in a 2017 final rule on the meaning of “intended use,” the FDA clarified that it will regulate products made or derived from tobacco as drugs or devices only when they are intended for disease treatment or prevention (e.g., if they are marketed with smoking cessation claims) or if they are marketed with claims, not commonly and legally made at the time *Brown & Williamson* was decided, that the product affects the structure or function of the body.¹²⁵

But, crucially, these limits on the agency’s flexibility to regulate *tobacco products* as drugs, devices, or drug-device combination products do not apply to synthetic nicotine products. Synthetic products are not made or derived from tobacco, so they are generally considered *not* to be tobacco products.¹²⁶ Additionally, many of the concerns about the application of the

¹²³ *Id.* at 893–94. The reasoning of *Sottera* was questionable. As discussed, the *Brown & Williamson Tobacco* decision focused on the unique history of tobacco and tobacco regulation. E-cigarettes are relatively new products without the unique history and economic importance of traditional tobacco. The Supreme Court certainly did not have e-cigarettes (which had not been introduced in the United States yet) in mind when it wrote its decision. See generally *Brown & Williamson*, 529 U.S. 120 (lacking any mention of e-cigarettes). Thus, the FDA could have reasonably concluded that *Brown & Williamson* did not constrain its discretion with regards to other nicotine-containing products. See generally *id.* Likewise, no evidence exists showing that Congress, when it passed the TCA, was thinking about e-cigarettes at all—and none that it intended for them to be regulated only as tobacco products.

¹²⁴ *Sottera*, 627 F.3d at 893–94.

¹²⁵ January 2017 FDA Clarification, *supra* note 55, at 2194, 2198, 2214. As discussed above, the FDA indefinitely delayed the effective date of other, contested aspects of this final rule. 2018 FDA Clarification, 83 Fed. Reg. 11,639, 11,639 (Mar. 16, 2018); see *supra* note 55 and accompanying text.

¹²⁶ See *Commonly Asked Questions*, *supra* note 14; Sarah Zhang, *supra* note 104; cf. *What Is TFN*, NEXT GENERATION LABS, <http://www.nextgenerationlabs.com/> [<https://perma.cc/5JGA-J5SM>] (marketing a product called TFN®, or “Tobacco Free Nicotine”). Because dietary supplements can be intended to affect structure or function of the body without becoming drugs under the law, it is also worth noting that synthetic nicotine products do not meet the definition of a dietary supplement. See 21 U.S.C. § 321(ff) (2012). Most importantly, the FDA has previously opined that products containing nicotine cannot be dietary supplements because dietary supplements cannot contain active ingredients that were approved or studied as drugs before being marketed as dietary supplements or foods. See *id.* § 321(ff)(3). Nicotine has been an active ingredient in approved NRT drugs since the early 1980s, well before both the enactment of the Dietary Supplement Health and Education Act of 1994, which created the modern scheme for regulating dietary supplements and any companies’ attempts to market nicotine-containing products as dietary supplements. See *Center for Drug Evaluation and Research 2002*, *supra* note 110. Even if nicotine was not an active ingredient in drugs, dietary substances must contain a “dietary ingredient,” and, in certain circumstances, the FDA takes the position that synthesized versions of naturally occurring dietary substances do not qualify as such. 21 U.S.C. § 321(ff)(1); see also U.S. FOOD &

FDA's drug authorities to tobacco products, which drove the majority's decision in *Brown & Williamson*, are not present for synthetic nicotine products.¹²⁷ If synthetic nicotine e-cigarettes live up to advocates' claims that they are a safe(r) way to use nicotine, these products should not provoke the same concern that they cannot satisfy the "safe and effective" standard needed for drug approval as cigarettes did.¹²⁸ Similarly, the synthetic nicotine industry is a nascent one, without the economic, social, and political significance of the tobacco industry that helped motivate the majority's conclusion in *Brown & Williamson* that Congress did not intend for the FDA to regulate tobacco products.¹²⁹ Finally, Congress explicitly chose to apply the TCA's requirements only to "tobacco products," declining to direct the FDA to regulate drugs containing nicotine, such as the smoking cessation products long regulated as drugs, under the new TCA scheme.¹³⁰ Therefore, unlike the FDA's attempt to regulate traditional tobacco products as drug-device combination products in the 1990's, the FDA regulating synthetic nicotine products as drugs would not raise concerns that the FDA was contravening the will of Congress.¹³¹

This means that, as with any other novel product, the FDA has considerable flexibility to determine whether a synthetic nicotine product falls within the drug definition.¹³² That is, the inquiry for determining whether a particu-

DRUG ADMIN., DRAFT GUIDANCE FOR INDUSTRY, DIETARY SUPPLEMENTS: NEW DIETARY INGREDIENT NOTIFICATIONS AND RELATED ISSUES 38 (2016), <https://www.fda.gov/downloads/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/UCM515733.pdf> [https://perma.cc/YY8J-LH69]. Thus, although nicotine naturally occurs in certain foods, such as tomatoes, synthetic nicotine may not be a dietary ingredient. See 21 U.S.C. § 321(ff)(1). Moreover, to be a dietary supplement, a product must be "intended for ingestion." *Id.* § 321(ff)(2)(A)(i). Currently marketed synthetic nicotine e-liquids are intended for inhalation, not ingestion.

¹²⁷ See *Brown & Williamson*, 529 U.S. at 133–61.

¹²⁸ See 21 U.S.C. §§ 355(d), 393(b)(2)(B).

¹²⁹ See *Brown & Williamson*, 529 U.S. at 172.

¹³⁰ See Family Smoking Prevention and Tobacco Control Act §§ 911(c), (g)(4), 918, Pub. L. No. 111-31, 123 Stat. 1776 (2009).

¹³¹ On the other hand, one might argue that the FDA choosing not to regulate synthetic nicotine products would contravene the will of Congress. Part of the rationale for Congress enacting the TCA was its recognition of the addictive nature of nicotine and the risks nicotine poses for youth, both concerns that apply to synthetic nicotine as forcefully as to tobacco-derived nicotine. Thus, the TCA might be viewed as evincing Congress's general intent that the FDA oversee all nicotine-containing products, even if Congress did not anticipate the development of a market of synthetic nicotine consumer products at the time the law was enacted. See generally *id.*

¹³² See *United States v. Bacto-Unidisk*, 394 U.S. 784, 793 (1969) (giving the FDA wide latitude in how it interprets the drug and device definitions in the FDCA); Peter Barton Hutt, *Philosophy of Regulation Under the Federal Food, Drug and Cosmetic Act*, 28 FOOD DRUG & COSMETIC L.J. 177, 178 (1973) (arguing that "the Act must be regarded as a constitution" that "establishes a set of fundamental objectives—safe, effective, wholesome, and truthfully-labeled products—without attempting to specify every detail of regulation").

lar synthetic nicotine product is a drug is the same as it is for any non-tobacco product. There is no need to consider whether the synthetic nicotine product is “customarily marketed,” nor are there any tobacco-specific limits on the agency’s authority to regulate synthetic nicotine products as drugs.

B. The Intended Use of Synthetic Nicotine

Because *Brown & Williamson* and *Sottera* do not apply to products that are not “tobacco products,” the determining factor for whether synthetic nicotine products are drugs is, simply, their intended use.¹³³ Although the precise rule for determining a drug’s intended use is currently the subject of debate,¹³⁴ a myriad of evidence may be relevant to the analysis.¹³⁵ Most clearly, a seller’s representations about its product might be evidence of the product’s intended use.¹³⁶ But the plain language of the statute, which describes uses as “intended” rather than “labeled,” “promoted,” or “claimed,” makes apparent that evidence other than a sellers’ representations can also be relevant.¹³⁷

¹³³ See *Brown & Williamson*, 529 U.S. at 172; *Sottera*, 627 F.3d at 894.

¹³⁴ See 2018 FDA Clarification, 83 Fed. Reg. 11,639, 11,639–41 (Mar. 16, 2018); Medical Information Working Group et al., Petition to Stay and for Reconsideration of Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products, 2–9 (Feb. 8, 2017), <https://www.regulations.gov/document?D=FDA-2015-N-2002-1977> [<https://perma.cc/4LXR-WF5C>]; see also Lewis A. Grossman, *Food, Drugs, and Droids: A Historical Consideration of Definitions and Categories in American Food and Drug Law*, 93 CORNELL L. REV. 1091, 1108 (2008) (“Indeed, modern food and drug law is bedeviled by the question of how the phrase ‘intended to’ in these definitions should be construed.”).

¹³⁵ See, e.g., *United States v. Storage Spaces Designated Nos. “8” & “49,”* 777 F.2d 1363, 1366 (9th Cir. 1985) (“This intent may be derived or inferred from labeling, promotional material, advertising, or any other relevant source.” (internal quotation marks omitted)).

¹³⁶ Grossman, *supra* note 134, at 1108.

¹³⁷ See 21 U.S.C. § 321(g)(1) (2012); see also *Brown & Williamson*, 529 U.S. at 170 (Breyer, J., dissenting) (“The FDCA . . . does not use the word ‘claimed’; it uses the word ‘intended.’”); *Storage Spaces*, 777 F.2d at 1366 (“This intent may be derived or inferred from labeling, promotional material, advertising, or any other relevant source.”); *Action on Smoking & Health v. Harris*, 655 F.2d 236, 239 (D.C. Cir. 1980) (“[I]t is well established ‘that the ‘intended use’ of a product, within the meaning of the Act, is determined from its label, accompanying labeling, promotional claims, advertising, and any other relevant source.”); *Nat’l Nutritional Foods Ass’n v. FDA*, 504 F.2d 761, 789 (2d Cir. 1974) (“[A] factfinder should be free to pierce all of a manufacturer’s subjective claims of intent . . . to find actual therapeutic intent on the basis of objective evidence”); *United States v. Article . . . Consisting of 216 Cartoned Bottles, More or Less, Sudden Change*, 409 F.2d 734, 739 (2d Cir. 1969) (“It is well settled that the intended use of a product may be determined from its label, accompanying labeling, promotional material, advertising and any other relevant source.”); *V.E. Irons, Inc. v. United States*, 244 F.2d 34, 44 (1st Cir. 1957) (“[W]e are free to look to all relevant sources in order to ascertain what is the ‘intended use’ of a drug, and are not merely confined to the labels on the drug or the ‘labeling.’ The legislative history of the 1938 Act makes this clear. Such also has been the undeviating opinion of the courts which have had occasion to deal with the issue.”); *United States v. Travia*, 180 F. Supp. 2d 115,

The available evidence for synthetic nicotine products suggests that there is a strong case for the FDA to conclude that these products fall within the FDCA's broad definition of a drug.¹³⁸ Companies' representations about their products, the design of the products, and the circumstances surrounding their distribution all support this conclusion, as described in detail below.¹³⁹ Moreover, when sellers have challenged the FDA's authority to regulate a product—or challenged the FDA's determination about which category a product falls within—courts have generally sided with the FDA.¹⁴⁰ Thus, even if one (or two) of the below-discussed sources of evidence about the intended uses of synthetic nicotine products were unpersuasive to

119 (D.D.C. 2001) ("Labeling is not exclusive evidence of the sellers' intent. Rather . . . 'it is well established that the intended use of a product, within the meaning of the [FDCA], is determined from its label, accompanying labeling, promotional claims, advertising, and any other relevant source.'") (quoting *Action on Smoking and Health v. Harris*, 655 F.2d 236, 239 (D.C. Cir. 1980)); *United States v. 250 Jars, etc., of U.S. Fancy Pure Honey*, 218 F. Supp. 208, 211 (E.D. Mich. 1963) ("In determining that a particular article was intended to be used as a drug, a court is not limited to the labels on such article or to the labeling which accompanies it, but may look at all relevant sources."); *aff'd sub nom., United States v. 250 Jars "Cal's Tupelo Blossom U.S. Fancy Pure Honey"*, 344 F.2d 288 (6th Cir. 1965); *United States v. Undetermined Quantities of an Article of Drug Labeled as "Exachol"*, 716 F. Supp. 787, 791 (S.D.N.Y. 1989) ("The FDA is not bound by the vendor's subjective claims of intent, but can find actual therapeutic intent on the basis of objective evidence. . . . This intent may be derived from the labelling [sic], promotional material, advertising or any other relevant source."); *United States v. 789 Cases of Latex Surgeons' Gloves*, 799 F. Supp. 1275, 1285 (D.P.R. 1992) ("All of the circumstances surrounding the promotion and sale of the product constitute the 'intent.' It is not enough for the manufacturer to merely say that he or she did not 'intend' to sell a particular product as a device."); *United States v. Vascular Sols., Inc.*, 181 F. Supp. 3d 342, 347 (W.D. Tex. 2016) (noting that non-public statements may be used as evidence of intended use); Grossman, *supra* note 134, at 1109 ("In the years immediately following [the enactment of the 1906 Pure Food and Drugs Act] . . . the FDA and the courts looked to evidence other than drug manufacturers' explicit claims to determine the 'intended use' of products."); *cf.* *United States v. An Article of Device*, 731 F.2d 1253, 1258 (7th Cir. 1984) ("[E]vidence showing that the TRD was used solely for research does not rebut the evidence that the device was intended for use in the treatment and diagnosis of disease.").

¹³⁸ See *infra* notes 143–210 and accompanying text.

¹³⁹ See *infra* notes 143–210 and accompanying text.

¹⁴⁰ See Adam Candeub, *Digital Medicine, the FDA, and the First Amendment*, 49 GA. L. REV. 933, 957 (2015); Patricia J. Zettler, *What Lies Ahead for FDA Regulation of tDCS Products*, 3 J.L. & BIOSCI. 318, 321 (2016). *But see* *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 28 (D.D.C. 1997) (rejecting the FDA's product classification because the agency's decision did not treat like products similarly). Additionally, categorizing synthetic nicotine products as drugs would be consistent with past FDA positions on products that similarly contain ingredients that are also commonly in non-drug products. For example, caffeine is in many foods such as coffee, but in certain circumstances the FDA has asserted that powdered caffeine products are drugs. See, e.g., Warning Letter from Michael Dutcher, Dir., FDA Minneapolis Dist., to Timothy Meyer, *alv* Supplement Direct (Mar. 3, 2016), <https://www.fda.gov/iceci/enforcementactions/warningletters/2016/ucm489374.htm> [<https://perma.cc/K5WK-55NR>] (describing caffeine powder as a drug).

courts, courts may be likely to agree with, or defer to, the agency's interpretation that a synthetic nicotine product is a drug.¹⁴¹

To be clear, determining a product's intended use is a product-specific inquiry. The features of the particular product at issue, including the seller's representations about the product, must be assessed individually.¹⁴² But in this Article, we do not take on the task of fully examining individual products or identifying specific products that meet the definition of a drug. Rather, we demonstrate that, based on the illustrative examples identified below, it appears that synthetic nicotine products generally fall within the drug definition.

1. Sellers' Representations

Sellers' claims that their products diagnose, cure, mitigate, treat, or prevent disease ("disease claims") or that their products affect the structure or function of the body ("structure/function claims") are, perhaps, the evidence that the FDA most commonly, and least controversially, relies on to determine a product's intended use.¹⁴³ These claims might come in the form of written statements or graphic representations in product labeling or advertising, including on websites or social media, or oral statements made by or on behalf of the seller.¹⁴⁴ Additionally, both disease and structure/function claims might be explicit or implicit. For example, "controls diabetes" is an explicit claim that a product treats diabetes, whereas "controls blood sugar" implies that a

¹⁴¹ See Zettler, *supra* note 140, at 321. The majority's conclusion in *Sottera* that the FDA was not owed deference because the question at issue in that case was not one of statutory interpretation, but rather one of interpreting *Brown & Williamson*, is not relevant to synthetic nicotine products because they are not tobacco products. See *Sottera*, 627 F.3d at 893–94.

¹⁴² See, e.g., Zettler, *supra* note 140, at 321.

¹⁴³ Cf. Medical Information Working Group et al., *supra* note 134, at 2 ("From the outset, the 'intended use' prong of the drug definition related to the seller's claims for its products."). In recent years, courts have become increasingly willing to find that the FDA's policies on "off-label" promotion of approved drug products, which rely on sellers' claims as evidence of intent, conflict with First Amendment protections for commercial speech. Christopher Robertson & Aaron S. Kesselheim, *Regulating Off-Label Promotion—A Critical Test*, 375 NEW ENG. J. MED. 2313, 2313–14 (2016). Scholars have expressed concern that if the logic of these decisions is extended, the entire structure of the FDCA—including, possibly, the reliance on sellers' claims as evidence of intended use for the purposes of defining a product—may be eroded. *Id.* at 2315. Courts, however, have thus far not concluded that the First Amendment protects the promotion of unapproved drugs or bars the FDA from considering sellers' representations in determining whether the FDA has jurisdiction over a product. For a general discussion of the First Amendment in the commercial speech context, see Victor Brudney, *The First Amendment and Commercial Speech*, 53 B.C. L. REV. 1153 (2012).

¹⁴⁴ Cf. Nathan Cortez, *The Statutory Case Against Off-Label Promotion*, 83 U. CHI. L. REV. ONLINE 124, 126 (2016), https://chicagounbound.uchicago.edu/ucirev_online/vol83/iss1/12/ [<https://perma.cc/K5WK-55NR>] (explaining the varied forms that prescription drug promotion takes).

product treats diabetes through referencing a characteristic sign of the disease.¹⁴⁵ Likewise, a structure/function claim might be implicit—as one example, “charge your mind” does not explicitly state that a product will enhance cognitive function, but implies that it will.¹⁴⁶

Reviewing the websites and social media accounts of synthetic nicotine product sellers suggests that sellers routinely make representations that the FDA could reasonably construe as either disease or structure/function claims. Smoking cessation claims are the most obvious kind of disease claims that purveyors of synthetic nicotine products might make.¹⁴⁷ This is because many consumers believe that e-cigarettes—whether using synthetic nicotine or nicotine derived from tobacco—are effective smoking cessation aids.¹⁴⁸

Consistent with this market potential, some sellers of synthetic nicotine products appear to represent their products as intended for smoking cessation. For example, the CEO of Vapeix, in a press release announcing its partnership with Next Generation Labs to develop products using synthetic nicotine, stated that “[t]his technology alliance will not only open the door for an entirely new, non-tobacco vape market, it aligns us closer to the pharmaceutical industry when combining the benefits from Vapeix Powered technologies with [synthetic nicotine], which can potentially result in future cessation tools for adult smokers.”¹⁴⁹ Indeed, in Next Generation Labs’ patent application for its method of synthesizing nicotine, it wrote that its

¹⁴⁵ See 21 C.F.R. § 101.93(g)(2)(ii) (2017); Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, 65 Fed. Reg. 1000, 1013 (Jan. 6, 2000) (to be codified at 21 C.F.R. pt. 101).

¹⁴⁶ Zettler, *supra* note 140, at 320.

¹⁴⁷ Cf. January 2017 FDA Clarification, *supra* note 55, at 2196, 2198–200 (explaining that smoking cessation claims are disease claims); Warning Letter from Gerald J. Berg, Dir., FDA Minneapolis Dist., to Christian Berkey, CEO, Johnson Creek Enters., LLC (Sept. 8, 2010), <https://wayback.archive-it.org/7993/20161023101826/http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2010/ucm225206.htm> [<https://perma.cc/JEU8-9XFG>] (same). For further discussion of smoking cessation claims as disease claims, see *supra* notes 58–59 and accompanying text.

¹⁴⁸ The evidence to support this assertion is mixed, and more research is currently underway. Compare Sara Kalkhoran & Stanton A. Glantz, *E-cigarettes and Smoking Cessation in Real-World and Clinical Settings: A Systemic Review and Meta-Analysis*, 4 LANCET RESPIRATORY MED. 116, 117 (2016) (concluding that “[a]s currently being used, e-cigarettes are associated with significantly less quitting among smokers”), with Shu-Hong Zhu et al., *E-cigarette Use and Associated Changes in Population Smoking Cessation: Evidence from US Current Population Surveys*, 358 BMJ 1, 5 (2017) (finding that “[t]he substantial increase in e-cigarette use among US adult smokers was associated with a statistically significant increase in the smoking cessation rate at the population level”).

¹⁴⁹ Press Release, Vapeix, Vapeix and Next Generation Labs Partner to Develop Connected Vape System (July 26, 2016), <https://www.vapeix.io/press-release-vapeix-next-generation-labs-partner-develop-connected-vape-system/> [<https://perma.cc/9BBS-3YTQ>].

product could be used “in vapor for treatment of smoking cessation [sic]”¹⁵⁰

That said, because it is well-known that the FDA considers smoking cessation claims to be evidence that any product, including a tobacco-derived nicotine product, is a drug, synthetic nicotine product sellers may avoid such claims. More common may be representations that synthetic nicotine products are less harmful than tobacco products. One seller’s blog, for example, states that their synthetic nicotine products contain “[n]o [c]arcinogenic or other tobacco combustion substances.”¹⁵¹ Similarly, another seller of synthetic nicotine products claims “since [its product] is completely synthetic, [it] does not contain any of some of the most harmful chemicals typically found as contaminants in tobacco-derived nicotine.”¹⁵² These kinds of statements would be “modified risk” claims if synthetic nicotine products were tobacco products—meaning these claims suggest the product reduces harm or the risk of tobacco-related disease—and would require FDA approval.¹⁵³ But outside of the context of tobacco products, modified risk claims are arguably disease claims. Although, on their face, modified risk claims are simply comparative claims about differences between synthetic nicotine and tobacco-derived nicotine products, they imply that synthetic nicotine products reduce the risk of disease and other health harms well known to be associated with tobacco and nicotine use.¹⁵⁴

Synthetic nicotine product sellers might also make disease claims unrelated to the diseases associated with the use of traditional tobacco products. For example, one seller of synthetic nicotine products posted on its Facebook page a customer review that touted the seller’s “glacier, minty menthol” flavor as “definitely something you vape when you’re like sick” with a cold because “it opens [you] up.”¹⁵⁵

¹⁵⁰ MICHAEL ARNOLD, NEXT GENERATION LABS, UNITED STATES PATENT APPLICATION PUBLICATION #US 2016/0115150 at AI (Apr. 28, 2016).

¹⁵¹ Danilo Delos Santos, *NTN—A New Generation of Nicotine*, HILIQ (Nov. 25, 2016) <http://blog.hiliq.com/ntn-a-new-generation-of-nicotine/> [<https://perma.cc/4P69-R8XZ>].

¹⁵² *TFN: Vape E-Liquid*, AUSTER, <https://www.auster.com/pages/tfn#> [<https://perma.cc/2RVK-AHAH>].

¹⁵³ See 21 U.S.C. § 387k (2012).

¹⁵⁴ Cf. Deeming Rule, 81 Fed. Reg. 28,974, 29,036–39 (May 10, 2016) (explaining why smoking cessation claims are not simply behavior modification claims, but are instead disease claims).

¹⁵⁵ SQN, FACEBOOK (July 19, 2017), <https://www.facebook.com/sqnvapor/> [<https://perma.cc/K3AG-4LBB>] (referring to no longer available video, Alexandra, *NKTR Ice E-Liquid—20% Off Code*, YOUTUBE (July 14, 2017), https://www.youtube.com/watch?v=RCA_42S4IV0); cf. digibomb, *Vaping While You’re Sick—Weekend Tip*, BIG VAPERS (Sept. 2, 2012), <https://bigvapers.wordpress.com/2012/09/02/vaping-while-youre-sick-weekend-tip/> [<https://perma.cc/MV7B-NF9K>] (asserting that, although smoking cigarettes exacerbated their cold symptoms, vaping menthol-flavored e-liquid “will help soothe” a sore throat and clear out sinuses).

But sellers of synthetic nicotine products perhaps most clearly represent their products as affecting the structure or function of the body. For instance, several sellers claim that their synthetic nicotine products have “the same biological impact as tobacco derived nicotine.”¹⁵⁶ This statement is an express structure/function claim by asserting that the product has a “biological impact” on the body. Moreover, by comparing synthetic nicotine to tobacco-derived nicotine—which is well known to be a stimulant and to be addictive—this statement would imply an effect on the structure or function of the body even without the “biological impact” language. Similarly, labeling products with different nicotine strengths, as many companies do, or claiming that one benefit of synthetic nicotine is that its flavor profile “allow[s] for the addition of a higher nicotine content,” implies that nicotine will affect the structure or function of the body.¹⁵⁷ If not, why have higher strengths of the ingredient, while also asserting that the nicotine lacks any taste or odor?¹⁵⁸ Even merely claiming nicotine as an ingredient, which all sellers of synthetic nicotine products seem to do, can be construed as a structure/function claim because of nicotine’s well-known impact on the body.¹⁵⁹ Indeed, nicotine’s impact on the body is also frequently described in warnings and disclaimers on the sellers’ websites.¹⁶⁰

In some circumstances, courts have appeared to conclude that structure/function claims must have some therapeutic implication to place a product within the FDA’s jurisdiction.¹⁶¹ To the extent such a limitation exists, however, it is not relevant to the kinds of structure/function claims that sellers

¹⁵⁶ *What Is TFN*, *supra* note 126; *see also* Santos, *supra* note 151; *TFN: Tobacco Free Nicotine*, EJUICE DIRECT, <https://ejuicedirect.com/collections/tfn-nicotine> [<https://perma.cc/N6CC-ACJK>]; *TFN Liquids*, VAPEREV, <https://www.vaperev.com/collections/tobacco-free-nicotine-e-liquids> [<https://perma.cc/LJB7-PZND>] (asserting that the product has the “[s]ame biological impact as . . . [t]obacco-derived [n]icotine”).

¹⁵⁷ *See TFN Liquids*, *supra* note 156; *see, e.g., What Is TFN*, *supra* note 126.

¹⁵⁸ *See, e.g., What Is TFN*, *supra* note 126.

¹⁵⁹ *Cf.* Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, 65 Fed. Reg. 1000, 1013 (Jan. 6, 2000) (explaining that describing a product with a commonly known drug name, such as “herbal Prozac,” can be construed as a disease claim).

¹⁶⁰ *See, e.g., Disclaimers*, NEXT GENERATION LABS, <http://www.nextgenerationlabs.com/disclaimers/> [<https://perma.cc/GPW6-867V>].

¹⁶¹ *See, e.g., United States v. Article . . . Consisting of 216 Cartoned Bottles, More or Less, Sudden Change*, 409 F.2d 734, 742 (2d Cir. 1969); *United States v. Article Consisting of 36 Boxes, More or Less, Labeled ‘Line Away Temp. Wrinkle Smoother,’* 415 F.2d 369, 372 (3d Cir. 1969); *United States v. Article of Drug 47 Shipping Cartons, More or Less, ‘Helene Curtis Magic Secret’* 331 F. Supp. 912, 916–17 (D. Md. 1971); Anna Wexler, *A Pragmatic Analysis of the Regulation of Consumer Transcranial Direct Current Stimulation (tDCS) Devices in the United States*, 2 J.L. & BIOSCI. 669, 690 (2015); Zettler, *supra* note 140, at 321.

make about their synthetic nicotine products.¹⁶² Courts have described structure/function claims with therapeutic implications to be those claims that suggest that a “product will affect the structure of the body in some medical- or drug-type fashion.”¹⁶³ Claims related to nicotine or a biological impact on the body would seem to easily meet this standard of a “drug-type” effect because nicotine is the active ingredient in drugs approved for smoking cessation,¹⁶⁴ and also because nicotine’s stimulant effects and additive properties are well known and similar to the effects of other drugs.¹⁶⁵

Synthetic nicotine companies, thus, appear to routinely represent their products as being intended to mitigate, treat, or prevent disease or to affect the structure or function of the body such that their products fall within the definition of a drug. Although some companies include statements on their website disclaiming any intent that synthetic nicotine products will diagnose, treat, cure, or prevent disease, such disclaimers may not be sufficient to correct the overall impression companies have created that synthetic nicotine products are intended for therapeutic use.¹⁶⁶ Moreover, on their face, these disclaimers do nothing to dispel the impression that synthetic nicotine products are intended to affect the structure or function of the body. The

¹⁶² As one of the authors has argued elsewhere, it is not clear that courts consider a therapeutic implication to be necessary outside the context of tobacco products. *See* Zettler, *supra* note 140, at 319 n.18; *see also* FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 162 (2000) (Breyer, J., dissenting). Moreover, the FDA has a long and established history of interpreting *pure* structure/function claims to cause products to fall within the definition of a drug (or the definition of a dietary supplement), to which courts may be likely to defer. *See generally* Chevron, U.S.A., Inc. v. Nat. Res. Def. Council, Inc., 467 U.S. 837 (1984) (establishing the principle of court deference to agency interpretation of its governing statute); Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, 65 Fed. Reg. 1000 (Jan. 6, 2000).

¹⁶³ *Sudden Change*, 409 F.2d at 742.

¹⁶⁴ *See, e.g.*, NICODERM LABELING (May 4, 2016), https://www.accessdata.fda.gov/drugs_atfda_docs/label/2016/20165Orig1s038lbl.pdf [<https://perma.cc/C2BB-WRTX>] (providing an example of labeling for a smoking cessation drug).

¹⁶⁵ *Cf.* alvSupplement Direct Warning Letter, *supra* note 140 (describing caffeine powder as a drug).

¹⁶⁶ *See, e.g.*, United States v. Storage Spaces Designated Nos. “8” & “49,” 777 F.2d 1363, 1366 n.5 (9th Cir. 1985) (concluding that products labeled as “incense” and “not for drug use” were drugs under the FDCA where the “overall circumstances” demonstrated the seller’s intent that products be used as cocaine substitutes); *Latex Surgeons’ Gloves*, 799 F. Supp. at 1285 (“All of the circumstances surrounding the promotion and sale of the product constitute the ‘intent.’ It is not enough for the manufacturer to merely say that he or she did not ‘intend’ to sell a particular product as a device.”); *Drug Labeled as “Exachol,”* 716 F. Supp. at 791 (“FDA is not bound by the vendor’s subjective claims of intent An article intended to be used as a drug will be regulated as a drug . . . even if the product’s labeling states that it is not a drug.”); January 2017 FDA Clarification, *supra* note 55, at 2199, 2203, 2212 (“FDA intends to view such disclaimers skeptically because . . . [i]n most cases . . . FDA does not believe that disclaimers will sufficiently mitigate consumer confusion due to the product’s claimed therapeutic benefit.”).

FDA, therefore, could reasonably conclude—based on companies’ representations—that synthetic nicotine products are drugs under the FDCA.

2. Product Design

As the above analysis shows, synthetic nicotine products are frequently marketed with disease or structure/function claims that cause them to fall within the definition of a drug. But even if current marketing were modified such that sellers’ claims did not make such claims, the design of synthetic nicotine products—and in particular the fact that the products contain nicotine—also provides evidence that these products are intended to affect the structure or function of the body.¹⁶⁷

Indeed, in various circumstances, the FDA has relied on a product’s ingredients or other aspects of its design to infer the seller’s intent that it be used to affect the structure or function of the body. Perhaps most relevant, the FDA made this argument to support its (later vacated) 1996 rule asserting jurisdiction over tobacco products.¹⁶⁸ In its jurisdictional statement accompanying the 1996 rule, the FDA explained both that nicotine, in fact, does affect the structure or function of the body—through its addictive, mood-altering, and weight-loss properties—and that tobacco sellers intend this outcome.¹⁶⁹ The agency based its conclusion about sellers’ intent on five central findings, three of which clearly relate to product design: that the

¹⁶⁷ It is worth noting that merely removing the kinds of claims discussed in Part II.B.1 may not be sufficient to demonstrate a new intended use for the products. *See supra* notes 143–166 and accompanying text. For example, in one case involving a prostaglandin derivative for eyelash growth, the Federal Circuit seemed to conclude that a company’s *past* claims that its product affected the structure of eyelashes were relevant to an intended use analysis because the company did not materially alter its product’s formulation or disavow its previous claims, but continued to make claims referencing eyelash structure, albeit implicit claims. *Allergan, Inc. v. Athena Cosmetics, Inc.*, 738 F.3d 1350, 1357 (Fed. Cir. 2013). Although it was a California law at issue in the case, rather than the FDCA, the California law incorporated provisions of the FDCA and the intended use analysis was the same as it would have been under the FDCA. *See id.* at 1355–57; *see also Latex Surgeons’ Gloves*, 799 F. Supp. at 1285 (“[W]hen a manufacturer has created a market for a product to be used as a device, he or she cannot avoid the reaches of the [FDCA] by stating that the product has a different—and non-regulated use. The Courts have recognized the ‘carry-over effect’ that is created by a manufacturer’s original representations about the product.”); *Drug Labeled as “Exachol,”* 716 F. Supp. at 791 (noting that “Courts have recognized that where years later customers purchase a product in reliance on the therapeutic claims of the previous literature marketed with that product, the court may use such literature to determine the intent in marketing the product despite a later disclaimer”).

¹⁶⁸ *See Brown & Williamson*, 529 U.S. at 125–26 (vacating the 1996 rule); *Nicotine in Cigarettes and Smokeless Tobacco Is a Drug and These Products Are Nicotine Delivery Devices Under the Federal Food, Drug, and Cosmetic Act; Jurisdictional Determination*, 61 Fed. Reg. 44,619, 44,630 (Aug. 28, 1996).

¹⁶⁹ *Nicotine in Cigarettes and Smokeless Tobacco Is a Drug and These Products Are Nicotine Delivery Devices Under the Federal Food, Drug, and Cosmetic Act*, 61 Fed. Reg. at 44,630.

biological effects of nicotine are “so widely known and accepted that it is foreseeable to a reasonable seller that cigarettes and smokeless tobacco . . . will be used by consumers for [those] purposes”; that sellers “design their products to provide consumers with a pharmacologically active dose of nicotine”; and “[a]n inevitable consequence of the design . . . is to keep consumers using [the products] by sustaining their addiction to nicotine.”¹⁷⁰

Although a majority of the Supreme Court ultimately concluded that the FDA lacked authority to regulate the nicotine in tobacco products as drugs in *Brown & Williamson*, that decision was based on the Court’s conclusion that, because of issues unique to tobacco products, Congress did not intend for the FDA to regulate tobacco products as drugs.¹⁷¹ The Court did not disagree with—or even opine on—the FDA’s use of product design as evidence of intended use.¹⁷² *Brown & Williamson*, therefore, does not preclude the FDA from relying on these sources as evidence of intended use.

Outside of the tobacco products context, although no court has squarely faced the issue of whether product design *alone* can be sufficient evidence of a drug intended use, courts have seemed open to the idea.¹⁷³ For example, in *United States v. Article . . . Consisting of 216 Cartoned Bottles, More or Less, Sudden Change*, a 1969 case about whether a wrinkle cream was a cosmetic intended only to affect appearance, or a drug intended to affect the structure or function of the skin, the Second Circuit opined that a skin cream would be a cosmetic rather than a drug if the seller “avoids . . . claiming to affect the structure or function of the skin in some physiological . . . way” and “no actual physical effect exists.”¹⁷⁴ By stating that the cream must have no physical effect in order to escape regulation as a drug, the Second Circuit suggested that a product’s design—whether it actually has a physical effect—may be sufficient to conclude that the product is a drug.¹⁷⁵ Similarly, in a case about whether a product was a vitamin or a drug, although the court did not agree with the FDA’s argument that all products with vitamin doses higher than the recommended daily intake were drugs, the Second Circuit did not reject the agency’s argument on the ground that

¹⁷⁰ *Id.* at 44,660–61. For a discussion of the other two factors—consumer intent and seller knowledge of consumer intent—see *infra* notes 190–210 and accompanying text.

¹⁷¹ See *Brown & Williamson*, 529 U.S. at 125–26.

¹⁷² *Id.* at 126–61; see also *Sottera*, 627 F.3d at 893–99.

¹⁷³ *Cf.* Grossman, *supra* note 134, at 1127 (“The Second Circuit acknowledged that the [FDA], in determining the ‘intended use’ of a product, could look not only at labeling, promotional material, and advertising, but also to ‘any other relevant source.’”).

¹⁷⁴ *Cartoned Bottles*, 409 F.2d at 742; see also Zettler, *supra* note 140, at 321 n.18 (discussing *Cartoned Bottles*).

¹⁷⁵ See *Sudden Change*, 409 F.2d at 742.

FDA could not consider product design, and specifically dosage.¹⁷⁶ Instead, the court rejected the agency's conclusion that consumers could not be using such high-dose products "for nutritional purposes."¹⁷⁷

Moreover, after *Brown & Williamson*, the FDA has continued to rely on aspects of product design as evidence of intended use outside the tobacco context in some circumstances.¹⁷⁸ For example, in one warning letter, sent in 2000 to a company marketing a product called "Rejuvenique," the FDA argued that because the product was designed to "provid[e] electrical current to various facial muscles to repeatedly contract them," it was intended to affect the structure or function of the body—and was a device—"even if no claims were made for its specific use."¹⁷⁹ In 2003, the FDA sent a warning letter to a company marketing "Avacor Hair Care System," explaining that it was a drug intended for the treatment and prevention of hair loss and for the promotion of hair growth, because of "the claims made . . . and the three individual products of which it is composed."¹⁸⁰ As a final example, in a 2010 warning letter to the distributor of "Magic Power Coffee," the agency asserted that the product was intended to prevent or treat disease or to affect the structure or function of the body in part because it contained an analogue of sildenafil, the active ingredient in Viagra.¹⁸¹ The agency noted that Viagra is "well known to have an effect on the structure or function of the body."¹⁸² To be clear, warning letters are not final agency action, nor are they general policy statements that provide the agency's official thinking or interpretation as a guidance document or regulation would.¹⁸³ Agency interpretations set out in warning letters are not likely to

¹⁷⁶ *Nat'l Nutritional Foods Ass'n*, 504 F.2d at 789.

¹⁷⁷ *Id.*

¹⁷⁸ See, e.g., January 2017 FDA Clarification, *supra* note 55, at 2208 (providing examples of when the FDA has relied on product design as circumstantial evidence of intended use).

¹⁷⁹ Warning Letter from Larry D. Spears, Acting Dir., Office of Compliance, FDA, to Salton, Inc. (July 12, 2000), <http://www.casewatch.org/fdawarning/prod/2000/salton.shtml> [<https://perma.cc/B755-JKZZ>]; see also Zettler, *supra* note 140, at 320 n.13 (discussing the same warning letter).

¹⁸⁰ Warning Letter from Jerome G. Woyshner, Dist. Dir., FDA, to Anthony Imbriolo, President, Glob. Vision Prods., Inc. (Apr. 3, 2003), <https://www.casewatch.org/fdawarning/prod/2003/globalvision.shtml> [<https://perma.cc/Z334-JG4Q>].

¹⁸¹ Warning Letter from Ronald M. Pace, Dist. Dir., FDA, to Peter Erlikh, Vice-President, INZ Distributors, Inc. (Aug. 23, 2010) [hereinafter INZ Distributors Warning Letter], <https://wayback.archive-it.org/7993/20170112004414/http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2010/ucm225432.htm> [<https://perma.cc/SC46-P7ND>]; see also Zettler, *supra* note 140, at 320 (discussing the same warning letter).

¹⁸² INZ Distributors Warning Letter, *supra* note 181.

¹⁸³ See *Holistic Candles & Consumers Ass'n v. FDA*, 664 F.3d 940, 943–44 (D.C. Cir. 2012); FOOD & DRUG ADMIN., REGULATORY PROCEDURES MANUAL § 4-1-1 (2017) ("Warning Letter Procedures").

receive deference from the courts.¹⁸⁴ Nevertheless, these warning letters demonstrate that the agency has continued to take the position that a product's design, including its ingredients, can be evidence of intended use, and has done so for products other than those containing nicotine. Moreover, the FDA recently affirmed the position staked out in these warning letters in its January 2017 revisions to the definition of "intended use."¹⁸⁵

Each of the arguments about product design that the FDA made in its 1996 jurisdictional statement regarding tobacco products apply with equal force to synthetic nicotine products—and possibly with even more force given greater scientific knowledge about the effects of nicotine today. As was true in 1996, the biological effects of nicotine are widely known and accepted, and it is foreseeable to reasonable synthetic nicotine sellers that consumers will use the products for those effects.¹⁸⁶ Sellers' disease and structure/function claims are evidence of this foreseeability—sellers anticipate that consumers will purchase their products for smoking cessation, harm reduction, or "biological impact," and seek to capitalize on that consumer interest through their marketing.¹⁸⁷ Sellers also design their synthetic nicotine products to provide an effect on the bodies of consumers, as evidenced by the presence of nicotine in the formulations, as well as the variation of nicotine strength in the different formulations.¹⁸⁸ These different strengths might also be evidence that a product is intended for use in smoking cessation or as a treatment for nicotine addiction because the different strengths, including the formulations with zero milligrams nicotine, may suggest that the consumers can decrease their nicotine use gradually until they use no nicotine at all.¹⁸⁹ Finally, just as with tobacco products, nicotine in synthetic products is addictive, and can be expected to keep consumers using the product (including at least some consumers who intend to quit using, but

¹⁸⁴ See, e.g., *Sottera*, 627 F.3d at 899 (Garland, J., concurring) (noting that some agency interpretations are not entitled to the deference that the court normally extends an agency's interpretations of its governing statute under *Chevron*).

¹⁸⁵ January 2017 FDA Clarification, *supra* note 55, at 2208.

¹⁸⁶ Of course, some products that are designed to have biological effects—such as caffeinated soda or winter jackets that keep consumers warm—are not regulated as drugs (or devices). This is because the FDCA's definition of a drug expressly excludes foods, see 21 U.S.C. § 321(g)(1) (2012), and because, as explained previously, the FDA has applied commonsense limitations to its interpretation of the drug and device definitions. See *supra* note 57 and accompanying text.

¹⁸⁷ See *supra* notes 143–166 and accompanying text.

¹⁸⁸ See, e.g., *What Is TFN*, *supra* note 126; cf. Margaret Gilhooley, *Tobacco Unregulated: Why the FDA Failed, and What to Do Now*, 111 YALE L.J. 1179, 1183 (2002) (arguing that "the deliberate addition of an addictive substance would have made the case for manufacturer intent much more straightforward" for tobacco products).

¹⁸⁹ Alternately, the no-nicotine formulations may be intended to be combined with flavorless formulations that contain nicotine.

are unsuccessful). Therefore, the design of synthetic nicotine products, and in particular the inclusion of nicotine as an ingredient, alone may be sufficient evidence of intent to affect the structure or function of the body or to treat disease.

3. Circumstances of Distribution

In addition to sellers' representations about synthetic nicotine and the design of the products themselves, the "circumstances surrounding the distribution" of synthetic nicotine may be evidence that sellers intend these products to treat disease or affect the structure or function of the body.¹⁹⁰ Specifically, consumer intent to use synthetic nicotine for its physiological effects may provide such evidence. Although consumer intent likely provides weaker evidence of synthetic nicotine products' intended use than sellers' representations or the product design, it is worth considering because, as numerous courts have explained, the FDA is permitted to consider "any . . . relevant source" to determine a product's intended use.¹⁹¹

Courts have not often faced the question of whether consumer intent is relevant to determining the sellers' intent, likely because firms almost always make relevant claims about their products. When courts have addressed this issue, they have concluded that "evidence of consumer intent is a 'relevant source'" for determining intended use when "such evidence is strong enough to justify an inference as to the vendors' intent"—meaning that consumers use the product "predominantly and . . . nearly exclusively with the appropriate intent."¹⁹² In at least one case, in 2001, *U.S. v. Travia*, a federal judge concluded that this standard was met.¹⁹³ *Travia* involved the prosecution, under the FDCA, of several individuals who sold nitrous oxide ("laughing gas") in balloons outside a rock concert in Washington, D.C.¹⁹⁴ Because the balloons were unlabeled and unadvertised, the government was unable to rely on the sellers' representations to demonstrate that nitrous ox-

¹⁹⁰ 21 C.F.R. § 201.128 (2017).

¹⁹¹ *United States v. Article . . . Consisting of 216 Cartoned Bottles, More or Less, Sudden Change*, 409 F.2d 734, 739 (2d Cir. 1969). For additional examples of cases making this point, see *supra* note 137 and accompanying text.

¹⁹² *Action on Smoking & Health v. Harris*, 655 F.2d 236, 239-40 (D.C. Cir. 1980); *see also* *United States v. Travia*, 180 F. Supp. 2d 115, 119 (D.D.C. 2001) (quoting the same language).

¹⁹³ *Travia*, 180 F. Supp. 2d at 116-17.

¹⁹⁴ *Id.* Nitrous oxide is not a controlled substance, which is likely why the government pursued the prosecution as a violation of the FDCA rather than the federal Controlled Substances Act, which is the more common avenue for prosecuting individuals selling recreational drugs. *See, e.g.*, DRUG ENFORCEMENT ADMIN., CONTROLLED SUBSTANCES (2018), https://www.deadiversion.usdoj.gov/schedules/orangebook/c_cs_alpha.pdf [<https://perma.cc/7ZBP-C9GW>].

ide was a drug as defined in the FDCA.¹⁹⁵ Nevertheless, Judge Thomas F. Hogan of the D.C. District Court agreed with the government's position that the nitrous oxide was a drug because "[l]abeling is not exclusive evidence of the sellers' intent"; rather, intended use may be determined from any source.¹⁹⁶ In the circumstances involved in *Travia*, "the environment provided the necessary information between buyer and seller"; the defendants, thus, did not need to label or advertise their product, and the government could demonstrate that the nitrous oxide was intended to affect the structure or function of the body.¹⁹⁷ Furthermore, Congress has arguably approved of, or acquiesced to, this interpretation of consumer intent as relevant to the intended use inquiry by not amending the definition in the wake of *Travia*, or in the time since the FDA promulgated its regulation defining "intended use" broadly enough to encompass consumer intent over forty years ago.¹⁹⁸

Although Judge Hogan characterized the facts of *Travia* as "obviously unique," synthetic nicotine presents a similarly compelling case for the relevance of consumer intent in determining intended use.¹⁹⁹ In its 1996 jurisdictional statement regarding tobacco, the FDA described consumer intent as relevant to its determination that nicotine was a drug.²⁰⁰ The agency noted evidence that "consumers use [tobacco products] predominantly for pharmacological purposes," and "sellers of [tobacco products] know that nicotine in their products causes pharmacological effects . . . and that consumers use their products primarily to obtain [these] effects."²⁰¹ The agency went on to cite data finding that the vast majority of tobacco product users (between seventy-seven and ninety-two percent) were addicted to nicotine and used tobacco products to satisfy cravings, and that a majority also used tobacco for other pharmacological purposes, such as relaxation (seventy percent of users aged ten to twenty-two years old).²⁰² Likewise, there is good evidence that consumers who use e-cigarettes do so predominantly for their pharmacological effects, including their perceived smoking cessation benefits.²⁰³ Numerous surveys of adult e-cigarette users suggest that the

¹⁹⁵ *Travia*, 180 F. Supp. 2d at 118–19.

¹⁹⁶ *Id.* at 119.

¹⁹⁷ *Id.*

¹⁹⁸ See Meaning of "Intended Uses," 41 Fed. Reg. 6719, 6911 (Feb. 13, 1976); cf. Cortez, *supra* note 144, at 141–42 (discussing congressional approval as one tool of statutory interpretation).

¹⁹⁹ *Travia*, 180 F. Supp. 2d at 119.

²⁰⁰ Nicotine in Cigarettes and Smokeless Tobacco Is a Drug and These Products Are Nicotine Delivery Devices Under the Federal Food, Drug, and Cosmetic Act Jurisdictional Determination, 61 Fed. Reg. 44,619, 44,630 (Aug. 28, 1996).

²⁰¹ *Id.*

²⁰² *Id.* at 44,635–36.

²⁰³ Zhu, *supra* note 148, at 1.

most common reasons for e-cigarette use are to quit or reduce smoking and to reduce health risks.²⁰⁴ Youth are less likely to use e-cigarettes to quit smoking, and instead—according to the 2016 Surgeon General’s Report—use e-cigarettes because of curiosity, flavorings/taste, and harm reduction compared to cigarettes.²⁰⁵ Harm reduction reflects consumers’ intent to use e-cigarettes for their physiological effects, specifically for disease prevention. Although consumers’ interest in e-cigarettes, because of their flavorings or taste likely does not reflect consumers’ intent to achieve pharmacological effects, curiosity may reflect that intent. Many teens may be curious about the physiological effects of nicotine, particularly in light of widespread media coverage and advertising campaigns alluding to these effects.²⁰⁶ Curiosity or experimentation, for example, is cited as a common reason for teens to initiate illicit drug use, a context in which curiosity almost certainly reflects an interest in experiencing the physiological effects of the product.²⁰⁷ Although the available research focuses on e-cigarettes generally, rather than synthetic nicotine products specifically, there is little reason to think that synthetic nicotine consumers—who typically are buying vaping products identical to those that tobacco-derived nicotine consumers buy—would have significantly different motivations.

The argument that consumer intent is relevant to the question of whether synthetic nicotine is a drug is the most controversial argument that we advance. As Lewis Grossman has explained, “[r]egulated industries contend that intended use is established solely by representations made in labeling, advertising, and other promotion. Conversely, the FDA maintains that it can look to the overall circumstances of distribution, foreseeable use [and] actual use . . . to determine a product’s intended use.”²⁰⁸ Indeed, the extent to which the FDA can rely on a company’s knowledge about how consumers use its product is an issue at the heart of the controversy over the FDA’s now partially delayed 2017 revisions to its regulations defining intended

²⁰⁴ Jessica K. Pepper & Noel T. Brewer, *Electronic Nicotine Delivery Systems (Electronic Cigarettes) Awareness, Use, Reactions and Beliefs: A Systematic Review*, 23 TOBACCO CONTROL 375, 375 (2014); Lila J. Finney Rutten et al., *Use of E-cigarettes Among Current Smokers: Associations Among Reasons for Use, Quit Intentions, and Current Tobacco Use*, 17 PREVENTATIVE MED. 1228, 1228–29 (2016).

²⁰⁵ 2016 SURGEON GENERAL’S REPORT, *supra* note 48, at 75.

²⁰⁶ See Duke et al., *supra* note 102, at 3–7.

²⁰⁷ See *Principles of Adolescent Substance Use Disorder Treatment: A Research-Based Guide*, NAT’L INST. ON DRUG ABUSE (Jan. 2014), <https://www.drugabuse.gov/publications/principles-adolescent-substance-use-disorder-treatment-research-based-guide/frequently-asked-questions/why-do-adolescents-take-drugs> [<https://perma.cc/B2YK-YKAD>].

²⁰⁸ Grossman, *supra* note 134, at 1108.

use.²⁰⁹ Nevertheless, even with a narrow view of when consumer intent is relevant, there is a reasonable argument that synthetic nicotine presents one of the rare circumstances in which consumer intent is probative of sellers' intent.

The FDA, then, has three alternative ways of establishing intended use—the sellers' representations about their products, the design of the products, and the circumstances of distribution—all of which support the conclusion that the FDA can regulate synthetic nicotine products as drugs. As suggested above, there may be stronger or weaker evidence with regard to the sellers' representations in any particular case, but the intentional decision to use nicotine and consumers' expectations with regard to the products will be constant across synthetic nicotine products (or at least those designed for use as e-liquids). In comparison to tobacco products (*Brown & Williamson*) and e-cigarettes containing tobacco-derived nicotine (*Sottera*), where the unique history of tobacco and the language of the TCA gave the courts pause, the arguments for regulating synthetic nicotine products as drugs are far more straightforward and compelling.

III. THE POLICY CASE FOR REGULATING SYNTHETIC NICOTINE PRODUCTS AS DRUGS

Based on the evidence demonstrating that synthetic nicotine products are generally intended to address disease or affect the structure or function of the body, there is a strong case that the FDA has the legal authority to regulate synthetic nicotine products as drugs. The fact that the FDA *can* regulate a particular product, however, does not mean that it will, or should. Indeed, the FDA often exercises its discretion not to enforce requirements for a variety of reasons, and this may be particularly common for innovative products.²¹⁰

²⁰⁹ See 2018 FDA Clarification, 83 Fed. Reg. 11, 639, 11,639 (Mar. 16, 2018); Medical Information Working Group et al., *supra* note 134, at 5–12.

²¹⁰ See, e.g., FOOD & DRUG ADMIN., DRAFT GUIDANCE FOR INDUSTRY: ENFORCEMENT POLICY REGARDING INVESTIGATIONAL NEW DRUG REQUIREMENTS FOR USE OF FECAL MICROBIOTA FOR TRANSPLANTATION TO TREAT *CLOSTRIDIUM DIFFICILE* INFECTION NOT RESPONSIVE TO STANDARD THERAPIES 4 (2016) [hereinafter FMT DRAFT GUIDANCE] (noting that the FDA may not enforce requirements where health care providers take other risk-mitigation steps); FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY AND FOOD AND DRUG ADMINISTRATION STAFF: MOBILE MEDICAL APPLICATIONS 16 (Feb. 2015) [hereinafter MOBILE MEDICAL APPLICATIONS GUIDANCE], <https://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf> [<https://perma.cc/QXH3-9SR4>] (noting that some devices do not warrant enforcement of FDA requirements due to low risk to public); *Laboratory Developed Tests*, FOOD & DRUG ADMIN. (Mar. 28, 2016), <https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitrroDiagnostics/LaboratoryDevelopedTests/default.htm> [<https://perma.cc/M478-E3MZ>] (noting that FDA did not enforce some requirements due to simplicity of the procedure and low risk).

In this section, therefore, we explore the question of whether the FDA *should* regulate synthetic nicotine products as drugs. We identify several reasons why regulating synthetic nicotine products as drugs would be beneficial and not unreasonably burdensome on industry. We conclude that, not only does the FDA have the authority to regulate these products as drugs, it would serve the FDA's public health mission—and the public—for it to do so, even when synthetic nicotine products are marketed without explicit smoking cessation claims.

A. Treating Like Products Similarly

It is a maxim in administrative law and theory that “like cases should be treated alike.”²¹¹ Such consistency is viewed as fair, and indicative of an impartial, rational decision-making process that provides predictability for regulated entities.²¹² This notion of consistency is codified in the Administrative Procedure Act, which permits courts to set aside “arbitrary” and “capricious” agency decisions²¹³—the paradigmatic example of which is a decision that treats like cases differently.²¹⁴

Allowing the subset of synthetically derived e-liquids to evade regulation, while regulating tobacco-derived e-liquids, may unfairly give synthetic nicotine products an advantage in the marketplace. Regulating synthetic nicotine as a drug would allow the FDA to achieve the policy goal of treating all nicotine-containing e-cigarettes and e-liquids—regardless of whether they are tobacco-derived or not—more similarly than it otherwise could. A court is not likely to find that the FDA acted arbitrarily and capriciously for excluding synthetic nicotine products from its scheme for tobacco regulation, because the way the statute and the courts have defined tobacco products gives the FDA a legitimate reason for doing so.²¹⁵ The FDA generally may not have the authority to regulate synthetic nicotine products as tobacco products under the TCA because the nicotine is not derived from tobacco, and the FDA does not have the authority to regulate as drugs tobacco-

²¹¹ Yoav Dotan, *Making Consistency Consistent*, 57 ADMIN. L. REV. 995, 1000 (2005); see also Christopher J. Walker, *How to Win the Deference Lottery*, 91 TEX. L. REV. SEE ALSO 73, 80 (2013) (“Consistency in agency interpretation should be given weight because it treats similarly situated parties the same, protects parties that rely on interpretations, and guards against arbitrary or capricious agency action.”).

²¹² See Dotan, *supra* note 211, at 999.

²¹³ 5 U.S.C. § 706(2)(A) (2012).

²¹⁴ See, e.g., *Etelson v. Office Pers. Mgmt.*, 684 F.2d 918, 926–27 (D.C. Cir. 1982); see also *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27 (D.D.C. 1997) (the FDA “must treat similar cases in a similar manner unless it can provide a legitimate reason for failing to do so”).

²¹⁵ See *supra* notes 103–114 and accompanying text.

derived e-liquids that are “customarily marketed” under *Sottera*.²¹⁶ Nevertheless, because there is no evidence that synthetic nicotine differs from tobacco-derived nicotine in its biological impacts on users, there is no scientific or public health rationale for treating the two categories of products differently.²¹⁷

The FDA’s schemes for regulating tobacco products and drugs are distinct, but they parallel each other in important ways. As is true for drugs, the FDA may deem tobacco products misbranded if their labeling is false or misleading or fails to comply with FDA requirements, such as failing to disclose the seller or product ingredients, or failing to include relevant warnings.²¹⁸ Similarly, the FDA may deem both drug and tobacco products adulterated if they are contaminated, manufactured in insanitary conditions, or manufactured through methods that do not comply with good manufacturing practices.²¹⁹ In short, both regulatory schemes are designed to ensure transparency, honesty, and safety.

Additionally, just as the FDA has a gatekeeping role for drugs, it now has such a role for tobacco products. “New tobacco products”—tobacco products “not commercially marketed as of February 15, 2007”—must be reviewed by the FDA before entering the market.²²⁰ The statutory standard for FDA authorization of a tobacco product is the public health standard discussed in Part I,²²¹ which includes of the agency considering “the risks and benefits to the population as a whole, including users and nonusers of tobacco products.”²²² For drugs, the statutory standard is framed differently—for approval, a drug must be shown to be safe and effective for its intended uses.²²³ But the difference between the “safe and effective” standard for approval for drugs and the “appropriate for the protection of the public health” standard for tobacco products may not be as drastic as it seems at first glance.²²⁴ The FDA has long interpreted the “safe and effective” standard to mean that the benefits of a drug must outweigh its risks in order for it to be approved.²²⁵ In making that determination, the FDA, if appropriate,

²¹⁶ See *supra* notes 103–114, 118–132 and accompanying text.

²¹⁷ See Santos, *supra* note 151.

²¹⁸ See 21 U.S.C. §§ 352, 387c.

²¹⁹ See *id.* §§ 351, 387b (2012).

²²⁰ *Id.* § 387j(a)(1).

²²¹ See *supra* notes 21–114 and accompanying text.

²²² 21 U.S.C. § 387j(c)(4).

²²³ *Id.* § 355(d).

²²⁴ See *id.* §§ 355(d); 387j(c)(2), 393.

²²⁵ See, e.g., U.S. FOOD & DRUG ADMIN., MEMORANDUM: PUBLIC HEALTH INTERESTS AND FIRST AMENDMENT CONSIDERATIONS RELATED TO MANUFACTURER COMMUNICATIONS REGARDING UNAPPROVED USES OF APPROVED OR CLEARED MEDICAL PRODUCTS 2 (Jan. 2017)

will consider the population health impacts of drugs, including their use in intended and unintended users.²²⁶ For example, when approving antibiotics for human or animal use, the agency generally considers the risk that inappropriate use of the drugs will contribute to antibiotic resistance, which is, of course, a grave threat to the public health.²²⁷ As another example, the agency required a special risk mitigation program for certain high-dose opioid products in formulations likely to appeal to children, such as lozenges and lollipops, in part to prevent accidental exposure in children, who are not intended users of the product.²²⁸ In other words, for appropriate drugs—such as synthetic nicotine products—the FDA has the flexibility to consider population health factors in its regulatory decision making, similar to those it considers for tobacco products.²²⁹

Moreover, to the extent that synthetic nicotine products are being marketed as—or are widely understood by consumers to be—smoking cessation aids, they should be treated the same as NRTs and other smoking cessation products that the FDA already regulates as drugs.²³⁰ Otherwise, synthetic nicotine companies will be able to make unverified health claims, skirt quality control regulations, and take other actions that give them an unfair advantage in the marketplace (and potentially threaten public health).

[hereinafter FDA MEMO], <https://www.regulations.gov/document?D=FDA-2016-N-1149-0040> [<https://perma.cc/XFA6-GSNA>] (follow “View Attachment” hyperlink).

²²⁶ See generally Patricia J. Zettler et al., *Implementing a Public Health Perspective in FDA Drug Regulation*, 73 FOOD & DRUG L.J. 221 (2018).

²²⁷ See *id.*

²²⁸ U.S. FOOD & DRUG ADMIN., TRANSMUCOSAL IMMEDIATE RELEASE FENTANYL (TIRF) RISK EVALUATION AND MITIGATION STRATEGY (REMS) 2 (2014), https://www.accessdata.fda.gov/drugsatfda_docs/remis/TIRF_2017-04-11_REMS_Document.pdf [<https://perma.cc/5JYK-RVPU>].

²²⁹ See Zettler et al., *supra* note 226. This is one reason that the drug review process is not likely to amount to a ban on synthetic nicotine products, particularly if synthetic nicotine products, and e-cigarette products in general, have the harm reduction benefits that advocates claim that they do. It is also worth noting that, along with the July 2017 announcement that the agency’s tobacco policy would focus on nicotine, the FDA also announced that it is delaying the effective date of certain requirements of the Deeming Rule for products on the market in 2016, when the rule was issued. See *FDA Comprehensive Plan*, *supra* note 1. FDA regulation of currently marketed synthetic nicotine products, thus, could be timed to parallel the implementation of requirements for currently marketed tobacco e-cigarette products.

²³⁰ Cf. Angelica LaVito, *FDA May Consider Over-the-Counter Regulation for E-cigarettes*, CNBC (Mar. 28, 2018, 4:06 PM), <https://www.cnbc.com/2018/03/28/fda-may-consider-over-the-counter-regulation-for-e-cigarettes.html> [<https://perma.cc/CTC5-QATF>] (quoting the FDA commissioner as saying that the agency is considering regulating certain e-cigarettes as over-the-counter drugs).

B. Protecting Consumers

The classic rationale for FDA regulation, and its premarket review authority for drugs in particular, is that the agency protects consumers and the public health by preventing harmful products—unsafe or ineffective products, or products that do not have a net benefit for the public health—from entering the market.²³¹ The need for this consumer protection arises because most drugs are “credence goods,” meaning their safety, effectiveness, and quality cannot be readily and easily evaluated by patients and prescribers.²³² This results in an information asymmetry. Prescribers and patients cannot access full information about the risks and benefits of a drug, and thus cannot make decisions that will force harmful or ineffective drugs from the marketplace.²³³ Although other markets may have similar characteristics, the potentially serious consequences of taking harmful or ineffective drugs is cited to justify the FDA’s role in this context.²³⁴

This rationale for the FDA’s drug authorities applies to synthetic nicotine products just as it applies to many traditional drugs. Consumers are not likely to be able to assess the veracity of sellers’ claims related to smoking cessation, harm reduction, and the biological impact of synthetic nicotine, nor will consumers be able to determine which products are more likely to pose risks or produce the benefits or biological effects that the consumer is seeking. Additionally, allowing synthetic nicotine products on the market without any FDA vetting may have negative, long-term consequences for consumers. For instance, unverified health claims may drive people towards using e-cigarettes with synthetic nicotine to quit smoking instead of using other therapies that may be more effective and pose fewer risks to cardiovascular and respiratory health. Similar to e-cigarettes with tobacco-derived nicotine, synthetic nicotine products may also serve as a pathway to cigarette use, increasing the risk that individuals who would not otherwise smoke will do so.²³⁵

More practically, the 2016 Deeming Rule lays out the public health case for applying the FDA’s tobacco products authorities to e-cigarettes,

²³¹ See, e.g., Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TEL. COMM. & TECH. L. REV. 345, 348 (2007) (explaining “premarket approval is understood primarily as a consumer protection measure”); *History*, FOOD & DRUG ADMIN. (Mar. 7, 2018), <https://www.fda.gov/aboutFDA/WhatWeDo/History/> [<https://perma.cc/3AN9-K8XQ>] (“The Food and Drug Administration is the oldest comprehensive consumer protection agency in the U.S. federal government”).

²³² Ariel Katz, *Pharmaceutical Lemons: Innovation and Regulation in the Drug Industry*, 14 MICH. TELECOMM. & TECH. L. REV. 1, 13 (2007).

²³³ *Id.*

²³⁴ *Id.*

²³⁵ See *supra* notes 91–95 and accompany text.

including tobacco-derived nicotine e-liquids.²³⁶ Because of the parallels between the regulatory regime for tobacco products and that for drugs, much of the same reasoning supports applying the FDA's drug authorities to synthetic nicotine. That is, regulating synthetic nicotine products as drugs would serve the same consumer protection purposes that regulating other e-cigarette products under the scheme for tobacco products does.

One major public health concern is that e-cigarettes appeal, and are widely available, to adolescents and young adults, who are at an age of particular susceptibility to initiation of nicotine use and addiction.²³⁷ Adding to this concern, FDA research, conducted with the Centers for Disease Control (CDC), found an 800% increase in e-cigarette use among high school students from 2011–2014, with e-cigarettes being the most commonly used tobacco product among that age group.²³⁸ Even though e-cigarettes are likely a less harmful way to use nicotine than smoking, nicotine use itself carries risks for the user, and particularly for minors—including interfering with neurological development, leading to long-term cognitive and mental health consequences.²³⁹ For e-cigarettes that are tobacco products, the FDA has several tools to address this public health issue, such as prohibiting the sale of e-cigarettes to minors, requiring certain warnings on product labeling, prohibiting characterizing flavors that attract youth users, and considering the potential impact on minors' use in the premarket review process.²⁴⁰ If synthetic nicotine products are not regulated by the FDA, however, it may create an easy pathway for minors to access e-liquids and e-cigarettes that they otherwise would not have, thwarting the public health goals of the Deeming Rule.²⁴¹ If, on the other hand, synthetic nicotine products were regulated as drugs, the FDA could take steps to make such products less accessible to minors. For example, if synthetic nicotine products were sold

²³⁶ Deeming Rule, 81 Fed. Reg. 28,974, 28,981 (May 10, 2016).

²³⁷ *Id.*

²³⁸ *Id.* at 28,984. More recent data shows that e-cigarette use among high school students continued to rise in 2015, but then declined precipitously in 2016 (from 16.0% to 11.3%). Jamal et al., *supra* note 90, at 600. Though the full reasons for this sudden decline are unclear, “[t]obacco prevention and control strategies at the national, state, and local levels likely have contributed to the reduction in use of certain tobacco products, including e-cigarettes, among youths . . .” *Id.*

²³⁹ See *supra* notes 30–52 and accompanying text.

²⁴⁰ TOBACCO CONTROL LEGAL CONSORTIUM, THE DEEMING REGULATION: FDA AUTHORITY OVER E-CIGARETTES, CIGARS, AND OTHER TOBACCO PRODUCTS 5 (2017), <http://www.publichealthlawcenter.org/sites/default/files/resources/tclc-fda-deemingreg-regulation-authority-Dec2016.pdf> [<https://perma.cc/T5SZ-HLCB>].

²⁴¹ Although about forty states now prohibit the sale of e-cigarettes to minors, many state laws may not apply to synthetic nicotine, depending how the definition of “tobacco product” is worded. See Kristy Marynak et al., *State Laws Prohibiting Sales to Minors and Indoor Use of Electronic Nicotine Delivery Systems—United States, November 2014*, 63 MORBIDITY & MORTALITY WKLY. REP. 1145, 1148 (2014).

over-the-counter (“OTC”) without a prescription, the FDA likely could require that synthetic nicotine products only be sold to adults OTC, similar to what the agency required for Plan B, the emergency contraceptive drug.²⁴² As with tobacco products, the FDA could also require warnings on the labeling for synthetic nicotine products and consider minors’ use in its pre-market review.²⁴³

Regulation can also help ensure that e-cigarettes are not more harmful than necessary. For instance, the FDA is currently looking into the issue of e-cigarette battery safety. E-cigarette battery explosions have caused gruesome and severe injuries in some cases.²⁴⁴ Additionally, poor manufacturing practices could allow metals and other contaminants to enter e-cigarette aerosols,²⁴⁵ and some e-liquid flavors may include ingredients that are particularly toxic (e.g., diacetyl).²⁴⁶ The Deeming Rule envisions the FDA’s premarket review of tobacco products as a means to protect consumers by preventing the sale of riskier products. Again, however, if synthetic nicotine products avoid any FDA regulation, this goal may be thwarted and consumers may have easy access to unreasonably risky products. If synthetic nicotine products were regulated as drugs, however, the FDA could use its pre-market review authority for drugs to address such concerns.

C. Encouraging Research and Innovation

Although the FDA is often described as serving a consumer protection function, its premarket review authority also serves an important function in motivating research that produces the information necessary to assess the

²⁴² LABELING FOR PLAN B (LEVONORGESTREL) TABLETS (2009), https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/021045s015lbl.pdf [<https://perma.cc/R8M2-J6BF>]. Due to the political controversy associated with emergency contraceptives, the FDA’s decision making with respect to minors’ access to OTC Plan B has a long, “bungl[ed]” history. Lisa Heinzerling, *The FDA’s Plan B Fiasco: Lessons for Administrative Law*, 102 GEO. L.J. 927, 928 (2014). The only relevant point for the synthetic nicotine context, however, is that the FDA’s drug authorities do give the agency some ability to limit minors’ access to particular drugs, where the data supports restricting access.

²⁴³ This is not an exhaustive list of the requirements that the FDA could impose under its drug authorities. For example, the FDA may also be able to regulate the flavors of synthetic nicotine products if there is data that flavors affect the safety and effectiveness of the products.

²⁴⁴ E.g., Patty Pan, *Exclusive: Man Severely Injured After E-cigarette Blows Up in His Face*, FOX5 (Sept. 8, 2015, 9:52 PM), <http://www.fox5dc.com/news/national/17391566-story> [<https://perma.cc/L8T2-KRUH>].

²⁴⁵ See, e.g., David Barboza, *China’s E-cigarette Boom Lacks Oversight for Safety*, N.Y. TIMES, Dec. 14, 2014, at A1.

²⁴⁶ Jessica L. Barrington-Trimis et al., *Flavorings in Electronic Cigarettes: An Unrecognized Respiratory Health Hazard?*, 312 JAMA 2493, 2493 (2014).

benefits and risks of products.²⁴⁷ Producing scientifically sound information about the effects of products is expensive and time-consuming.²⁴⁸ Without a requirement that sellers demonstrate to the FDA that their drugs are safe and effective, or that marketing their tobacco products is appropriate for the protection of the public health, companies are not likely to rigorously study the effects of their products.²⁴⁹ The dietary supplement industry provides a salient example of the consequences of restricting the FDA's regulatory role. The claims that sellers make about dietary supplements, which are not subject to the FDA's premarket review, are rarely supported by rigorous scientific evidence.²⁵⁰

²⁴⁷ See Eisenberg, *supra* note 231, at 348; see also FDA MEMO, *supra* note 225, at 3 ("The FDA Authorities, among other things, motivate the development of scientific evidence that enables the reliable, population-level determination of the safety and efficacy of medical products for each intended use"); Erika Lietzan, *The Myths of Data Exclusivity*, 20 LEWIS & CLARK L. REV. 91, 150 (2016) ("some provisions that are viewed as more traditional health-and-safety measures also implement, whether intentionally or incidentally, innovation policy"); W. Nicholson Price II, *Making Do in Making Drugs: Innovation Policy and Pharmaceutical Manufacturing*, 55 B.C. L. REV. 491, 493 (2014) ("the FDA's regulatory barriers create carefully calibrated incentives for firms to discover and develop drugs"); Christopher Robertson, *When Truth Cannot Be Presumed: The Regulation of Drug Promotion Under an Expanding First Amendment*, 94 B.U. L. REV. 545, 561 (2014) ("[T]he FDCA does not exist to police the truth. Instead, the FDCA exists to provide and protect an epistemic and economic process of research and discovery . . ."); Rachel Sachs, *Delinking Reimbursement*, MINN. L. REV. (forthcoming 2018) ("A more modern view of the FDA . . . conceives of [it] as an information-producing, innovation-focused agency."), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3117069 [<https://perma.cc/38YN-ZM6R>].

²⁴⁸ See, e.g., Rick Mullin, *Tufts Study Finds Big Rise in Cost of Drug Development*, CHEMICAL & ENGINEERING NEWS (Nov. 20, 2014), <https://cen.acs.org/articles/92/web/2014/11/Tufts-Study-Finds-Big-Rise.html> [<https://perma.cc/T87L-9B7L>].

²⁴⁹ Cf. Christopher Robertson & Victor Laurion, *Tip of the Iceberg II: How the Intended-Uses Principle Produces Medical Knowledge and Protects Liberty*, 11 N.Y.U. J.L. & LIBERTY 770, 774 (2017) ("The FDCA requires a drugmaker to internalize the cost of scientifically investigating the safety and efficacy of its own product . . .").

²⁵⁰ See, e.g., DANIEL R. LEVINSON, OFFICE OF INSPECTOR GEN., DEP'T HEALTH & HUMAN SERVS., OEI-01-11-00210, DIETARY SUPPLEMENTS: STRUCTURE/FUNCTION CLAIMS FAIL TO MEET FEDERAL REQUIREMENTS (Oct. 2012), <https://oig.hhs.gov/oei/reports/oei-01-11-00210.asp> [<https://perma.cc/7JRK-6WK5>]. See generally PAUL A. OFFIT, DO YOU BELIEVE IN MAGIC?: VITAMINS, SUPPLEMENTS, AND ALL THINGS NATURAL: A LOOK BEHIND THE CURTAIN (2013) (discussing the relationship between claimed and actual effects in the vitamin industry). Not only are the safety and effectiveness claims about dietary supplements often unsupported, a significant percentage of supplements have been found not to contain the dietary ingredients their labeling lists as ingredients. Additionally, supplements, particularly those marketed for sexual enhancement, weight loss, and athletic performance enhancement, are frequently tainted with active pharmaceutical ingredients. See, e.g., Steven G. Newmaster et al., *DNA Barcoding Detects Contamination and Substitution in North American Herbal Products*, 11 BMC MED., Oct. 11, 2013, at 1, 10–11, <https://bmcmecine.biomedcentral.com/track/pdf/10.1186/1741-7015-11-222> [<https://perma.cc/XA4K-NAYS>]; JASON HUMBERT & NICOLE KORNSPAN, FOOD & DRUG ADMIN., TAINTED PRODUCTS MARKETING AS DIETARY SUPPLEMENTS 11 (2017), <https://www.fda.gov/downloads/AboutFDA/WorkingatFDA/FellowshipInternshipGraduateFacultyPrograms/PharmacyStudentExperientialProgramCDER/UCM585850.pdf> [<https://perma.cc/9TEF-HHNA>].

Using FDA oversight to motivate research into the effects of e-cigarettes and other novel nicotine products is a particularly important public health goal. There is significant hope (and, perhaps, hype) about the potential for e-cigarette use to reduce the harm associated with the use of traditional tobacco products, such as cigarettes—which are still the leading cause of preventable death in the United States. Although e-cigarettes seem to be less harmful than cigarettes, research, and particularly long-term studies, are needed to understand whether they provide a net benefit to the public health, what e-cigarette characteristics and marketing practices are likely to maximize public health benefits, and what unique harms (if any) may be associated with e-cigarette use.²⁵¹ Likewise, such research will be needed for other novel nicotine products that may enter the market.²⁵² Indeed, the FDA asserted that motivating research was one purpose served by its decision to promulgate the Deeming Rule.²⁵³ As the FDA explained, applying the agency's tobacco authorities to e-cigarettes “will provide FDA with critical information regarding the health risks of the products,” which “is particularly important given the addictiveness of nicotine and the toxicity associated with tobacco products.”²⁵⁴

Relatedly, regulating synthetic nicotine products as drugs may promote high-value innovation—in that it would require sellers to produce products for which there is reasonable certainty that the products will do what sellers claim they will do.²⁵⁵ That is, regulating synthetic nicotine products as drugs provides the opportunity for the FDA to not only encourage research, but also incentivize the development and sale of innovative synthetic nicotine products that deliver on industry's promise of a safe, or at least less harmful, way to use nicotine, just as the FDA can do for those e-cigarettes that are tobacco products. FDA gatekeeping serves, as one scholar has explained, as an “anti-lemon” mechanism.²⁵⁶

If, however, synthetic nicotine products are not subject to any FDA oversight, it is likely that synthetic nicotine will come to dominate the e-

²⁵¹ See, e.g., Deeming Rule, 81 Fed. Reg. 28,974, 28,984 (May 10, 2016); NAT'L ACADS. OF SCI., ENG'G & MED., *supra* note 91, at 481-85, 653-56 (identifying research needs).

²⁵² Cf. *Zia Gum*, *supra* note 105 (describing a recreational synthetic nicotine gum).

²⁵³ See Deeming Rule, 81 Fed. Reg. at 28,984.

²⁵⁴ *Id.*

²⁵⁵ See Daniel Carpenter et al., *Approval Regulation and Endogenous Consumer Confidence: Theory and Analogies to Licensing, Safety, and Financial Regulation*, 4 REG. & GOVERNANCE 383, 398 (2010); see also Nathan G. Cortez et al., *FDA Regulation of Mobile Health Technologies*, 371 NEW ENG. J. MED. 372, 376 (2014) (“The true challenge, however, is creating a regulatory framework that encourages high-value innovation while also preventing the market from being overcome with products that are ineffective or unsafe.”).

²⁵⁶ Katz, *supra* note 232, at 17.

cigarette market. If the majority of e-cigarettes fall outside FDA regulation, this result would be a lost opportunity to motivate industry to conduct rigorous research to answer the important questions about their products and to incentivize the creation of innovative e-cigarettes that truly reduce harm. But regulating synthetic nicotine as a drug would retain the information and innovation-producing benefits of FDA oversight—because sellers of synthetic nicotine products would need to produce rigorous scientific evidence about their products to obtain FDA authorization for marketing.

D. Considerations for Implementation

To realize many of these policy benefits, it is important that the FDA thoughtfully implement its regulation of synthetic nicotine products as drugs. Perhaps most obviously, the suggestion that synthetic nicotine products be regulated under the FDA's drug authorities is likely to produce objections that such regulation would be unduly burdensome, possibly even eliminating the burgeoning synthetic nicotine industry altogether. Indeed, these are common concerns about the FDA's decision to deem e-cigarette products subject to its tobacco authority, and the FDA's drug authorities are likely to be viewed as at least as onerous, if not more so, than its tobacco authorities.²⁵⁷

The FDA's drug authorities do impose burdens on regulated industry, including the often long process of developing safety and effectiveness information for approval, as well as labeling, promotion, and manufacturing requirements. To the extent that e-cigarettes or e-liquids, including synthetic nicotine, hold real promise for reducing the harm associated with tobacco and nicotine use, unreasonable burdens on industry should concern industry and consumer advocate stakeholders alike. The key, then, may be finding a way to achieve the policy benefits of regulating synthetic nicotine as a drug while assuring that the burdens are not unreasonable. Although we do not claim to identify the solution for achieving this balance (nor do we claim that the burden of regulation is the only important implementation question) we note that there are several ways that the FDA might streamline the process to market for synthetic nicotine products while preserving the benefits of regulating synthetic nicotine as a drug.²⁵⁸

²⁵⁷ See, e.g., Michael B. Siegel, *The FDA's Vaporous Thinking About E-Cigs*, WALL ST. J. (May 5, 2016), <https://www.wsj.com/articles/the-fdas-vaporous-thinking-about-e-cigs-1462487690>.

²⁵⁸ For example, if synthetic nicotine products were regulated as OTC drugs, it would be important that the FDA work with state regulators to consider how such FDA regulation intersects with state regulation of e-liquids, including considering issues of preemption that may arise. Cf. 21 U.S.C. § 379r (2012) (expressly preempting certain state requirements for non-prescription drugs).

One option might be for the FDA to exercise its discretion not to enforce certain drug requirements applicable to synthetic nicotine products. Exercising enforcement discretion is a tool that the agency has used to tailor its regulatory scheme for a number of other innovative technologies, including mobile medical apps, fecal microbiota transplantation, and certain genetic tests.²⁵⁹ Similarly, for synthetic nicotine products, if the scientific evidence supported such an approach, the FDA might decide not to enforce premarket review requirements for products that were not marketed as smoking cessation aids and were substantially equivalent to legally marketed tobacco products (with the only difference being synthetic nicotine in place of tobacco-derived nicotine). Such an approach, if consistent with how the FDA treated e-cigarettes regulated as a tobacco product and supported by sound scientific evidence, may enable synthetic nicotine products to reach the market quickly without sacrificing other benefits or goals of FDA regulation.

As Eric Lindblom has suggested for e-cigarettes subject to the FDA's tobacco-related jurisdiction, another option would be to promise expedited premarket review (and presumptive approval) to companies that agreed to take actions likely to reduce potential negative public health consequences associated with e-cigarette use.²⁶⁰ For example, companies could agree to market their products only to adults who are currently smokers, to include labeling or warnings explaining the dangers of dual use, and to conduct certain types of postmarket surveillance. Although this approach may raise concerns about the FDA's ability to enforce such industry commitments, it may be an appropriate option if the potential of e-cigarettes, including synthetic nicotine products, to provide significant public health benefits is demonstrated.²⁶¹

²⁵⁹ FMT DRAFT GUIDANCE, *supra* note 210, at 4; MOBILE MEDICAL APPLICATIONS GUIDANCE, *supra* note 210, at 16; ; U.S. Food & Drug Admin., *Laboratory Developed Tests*, *supra* note 210; *see also* Diane Hoffman et al., *Improving Regulation of Microbiota Transplants*, 358 SCIENCE 1390, 1390–91 (2017) (describing FDA regulation of fecal microbiota transplantation); Rachel Sachs & Carolyn A. Edelstein, *Ensuring the Safe and Effective FDA Regulation of Fecal Microbiota Transplantation*, 2 J.L. BIOSCI. 396, 400–08 (2015) (same); Margaret Foster Riley & Bernat Olle, *FDA's Pathway for Regulation of FMT: Not So Fraught*, 2 J.L. BIOSCI. 742, 742–46 (2015) (same).

²⁶⁰ Eric N. Lindblom, *Effectively Regulating E-cigarettes and Their Advertising—And the First Amendment*, 70 FOOD & DRUG L.J. 55, 75–76 (2015).

²⁶¹ The FDA, historically, has faced challenges enforcing premarket commitments made by pharmaceutical companies. *See, e.g.*, Kevin Fain et al., *The Food and Drug Administration Amendments Act and Postmarketing Commitments*, 310 JAMA 202, 202–03 (2013); U.S. DEP'T HEALTH & HUMAN SERVS., OEI-04-11-00510, OFFICE OF INSPECTOR GENERAL, FDA LACKS COMPREHENSIVE DATA TO DETERMINE WHETHER RISK EVALUATION AND MITIGATION STRATEGIES IMPROVE DRUG SAFETY 14–22 (Feb. 2013).

Finally, particularly because it seems likely that synthetic nicotine products would be marketed as OTC drugs, rather than drugs requiring a prescription, the FDA also might have options for allowing the marketing of synthetic nicotine products without requiring a product-by-product review.²⁶² The vast majority of OTC drugs are marketed pursuant to an “OTC Monograph”—a regulation promulgated by the FDA that establishes the conditions under which the FDA will consider a drug to be generally recognized as safe and effective, and not misbranded, such that it can be marketed without premarket approval.²⁶³ Although the OTC Monographs are generally available only to drugs that were marketed when the FDA began its systematic review of OTC drugs in 1972, there is a mechanism for adding later-introduced drugs to the monograph process.²⁶⁴ Through this mechanism, it might be possible to create an OTC Monograph for synthetic nicotine products, once more data is available about the conditions under which synthetic nicotine products are safe and effective.

This list does not exhaust the options that the FDA may have for reducing the burdens of regulation on synthetic-nicotine-product sellers, and determining what approaches may be appropriate deserves more detailed consideration than this Article can provide. But these examples do show that claims that FDA regulation necessarily will unreasonably burden the synthetic nicotine industry are not persuasive. Moreover, although all burdens associated with FDA regulating synthetic nicotine products as drugs cannot be eliminated, importantly those burdens may have numerous benefits, including enabling the agency to treat like products similarly, protecting consumers, incentivizing rigorous studies of synthetic nicotine, and encouraging beneficial innovation in this space.

CONCLUSION

The current regulatory gap for synthetic nicotine products—wherein tobacco-derived nicotine products are subject to FDA regulation and synthetic nicotine products are not—may prompt more and more companies to “mak[e] business choices on the basis of the difference between the two regulatory

²⁶² 21 U.S.C. § 353(b)(1); *see also* LaVito, *supra* note 230 (quoting the FDA commissioner as saying the agency is exploring regulating some e-cigarettes with tobacco-derived nicotine as OTC drugs). Many currently marketed drugs that contain nicotine, such as gums, lozenges, and transdermal patches intended as smoking cessation aids, are marketed OTC.

²⁶³ *See, e.g.*, U.S. Food & Drug Admin, Over-the-Counter Drug Monograph System—Past, Present, and Future; Public Hearing, 79 Fed. Reg. 10,168, 10,169 (Feb. 24, 2014).

²⁶⁴ *See* U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: TIME AND EXTENT APPLICATIONS FOR NONPRESCRIPTION DRUG PRODUCTS 2–16 (Sept. 2011), <https://www.fda.gov/downloads/drugs/guidances/ucm078902.pdf> [<https://perma.cc/RBH2-WC96>].

domains.”²⁶⁵ Such “regulatory arbitrage” serves no public health purpose and threatens to undermine the FDA’s newly announced “comprehensive plan for tobacco and nicotine regulation”²⁶⁶ There is, however, a fix available: the FDA can regulate synthetic nicotine products as drugs. This solution is not perfect; ideally, all nicotine-containing products (or at least all nicotine-containing e-liquids) would be subject to the same regulatory scheme, regardless of the source of the nicotine. But, as demonstrated in this Article, this approach is legally sound and, with thoughtful implementation, would promote the public’s interest in sound regulation and consumer protection, without sacrificing innovation. The FDA is poised to begin a promising new phase of tobacco and nicotine regulation; synthetic nicotine products, if properly regulated as drugs, could play a key role in the FDA’s effort to transition current smokers to less harmful nicotine products.

²⁶⁵ Nicolas P. Terry, *Regulatory Disruption and Arbitrage in Health-Care Data Protection*, 17 YALE J. HEALTH POL’Y, L., & ETHICS 143, 156 (2017).

²⁶⁶ *FDA Comprehensive Plan*, *supra* note 1.